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THE JOURNAL

OF THE

American Medical Association

Subscription, $8.00 | PUBLISHED WEEKLY | Single Copies, 25 Cents

VOLUME 115, No. 1

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535 North Dearborn Street, Chicago, Ill.

JULY 6, 1940

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On page 3 of this Journal you will find the complete contents of the *July Number* of the "Medical Clinics of North America" (from the Mayo Clinic). The Symposium deals with the *Present Status of Endocrine Therapy* and in addition there are included *14 other excellent clinical discussions* of current interest.

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association, 535 North Dearborn Street, Chicago, Ill. Subscription price, $8.00 a year. 25c a copy. Canadian $9.50. Foreign $12.00. Entered as second class matter June 25, 1885, at the Postoffice at Chicago, Ill., under Act of March 3, 1879.

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The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 115, No. 1

COPYRIGHT, 1940, BY AMERICAN MEDICAL ASSOCIATION

CHICAGO, ILLINOIS

JULY 6, 1940

CARBON MONOXIDE—A DOMESTIC HAZARD

WITH ESPECIAL REFERENCE TO THE PROBLEM IN WEST VIRGINIA

HARVEY G. BECK, M.D.
WILMER H. SCHULZE, PHAR.D.
AND
GEORGE M. SUTER, M.D.
BALTIMORE

As a cause of accidental and suicidal death carbon monoxide ranks second to automobile fatalities. It is estimated that there occur annually in the United States about fifty thousand deaths from asphyxiation, at least half of which are due to this gas. In New York City reports show that for every seven automobile deaths there are five carbon monoxide deaths. Unfortunately, there are few reliable statistics available on the incidence of acute carbon monoxide asphyxiation, and there are none whatever regarding the remote effect of the gas. The most valuable data have been collected and published by the Ohio State Board of Health, which has been emphasizing the importance of the subject from the standpoint of public health for a number of years. The records for 1936 showed a progressive increase of the hazard in both the domestic and the industrial life of the community.

Of a total of 518 gassings, there were 288 from defective domestic appliances, with sixty-two fatalities. Of the victims twenty-three were overcome by bathroom heaters with four deaths, twenty-six by hot water heaters with six deaths, and fifty-five by coal or coke stoves and furnaces with five deaths. The worst menace was the gas stove for heating rooms, which was responsible for twenty deaths. Even the beauty shop is not free from hazard, as eight persons were overcome from imperfect heating devices.

Despite the well known fact that carbon monoxide is a powerful death-dealing agent in acute asphyxiation, knowledge is lacking concerning the delayed result or after-effects of acute asphyxiation or the insidious effect of the gas in producing chronic ailments in those exposed intermittently over long periods. Years ago a statement to the effect that if carbon monoxide does not kill it will do no harm became axiomatic. Unfortunately, absurd as this statement seems, apparently no effort has been made to prove or disprove its correctness. In consequence, victims who have survived asphyxiation and become physically incapacitated have failed to get compensation for disability, nor did the family receive any award in case of death.

Read before the Scientific Society of the University of West Virginia, Oct. 27, 1939.

It is difficult to estimate the incidence of the so-called chronic forms or secondary syndromes of asphyxiation resulting from carbon monoxide. Until further clinical investigations are made and more careful statistics compiled, it can only be a matter of conjecture.

A personal study and analysis of 150 selected patients suffering either from anoxemia due to slow asphyxiation or from the residual effects of severe acute asphyxiation yielded important facts relating to the subject.

Geographically, the cases were distributed as follows: West Virginia ninety-six, Maryland forty-two, Pennsylvania five, Ohio four, Kentucky, New Jersey and Oklahoma one each.

In our series one out of eleven patients admitted from West Virginia for diagnosis was a victim of slow gas asphyxiation, whereas from all other states combined there was approximately only one out of every 150 patients.

There were ninety-one males and fifty-nine females. In West Virginia the distribution of sex was almost equal, forty-nine males and forty-seven females, while in Maryland there were thirty-two males and only ten females. This difference is attributed to the fact that in Maryland less gas is consumed for heating homes, stores, offices and school rooms, where women are largely employed. Besides, in Baltimore there is an ordinance restricting the sale of gas appliances for domestic use to those approved by sanitary engineers.

Of the group ninety-one were victims of natural gas, twenty-eight of manufactured or illuminating gas, and nineteen of automobile exhaust gas. There were six instances of exposure to both automobile and natural gas and two to automobile and illuminating gas. In four instances the source was coke or coal and blast furnaces.

Among the ninety-six patients from West Virginia five were without occupation. Included in a list of occupations were thirty-three housewives and domestic servants, nine merchants and office employees, nine teachers, eight physicians, six students, three restaurateurs, two attorneys and one minister—a total of seventy-six, or approximately 80 per cent, engaged in nonindustrial pursuits. This is in striking contrast to the situation in Maryland, which is more of an industrial community and where comparatively little natural gas is used for domestic purposes. Among the forty-two patients residing in Maryland there were only three housewives, one physician, one teacher, no students, seven merchants and office employees, one restaurateur, one minister and one attorney — a total of fifteen, or approximately 38 per cent, engaged in nonindustrial pursuits. By occupation, iron, tin and steel mill workers, service men in garages, auto repair men, taxicab drivers and tailors comprised 50 per cent of the patients. These studies furthermore revealed that diseases of the central nervous system, cardiovascular system and gastro-

intestinal system are much more common in persons whose occupations expose them to carbon monoxide over considerable periods of time. Thus in the series of 150 patients studied there were thirteen with symptoms of encephalitis, nine with epilepsy, three with multiple sclerosis and two with tetany. Besides, there were four patients in whom brain tumor was suspected and a number exhibiting marked psychotic and psychoneurotic manifestations.

Vienna records show that laborers engaged in occupations in which they are exposed to carbon monoxide suffer two and one-half times as much from gastrointestinal diseases as those not exposed. The Leipzig statistics show that nearly twice as many become ill and that the number of days for sick leave on account of digestive diseases increased 50 per cent. There is ample clinical evidence to indicate a similar increase in diseases of the heart and blood vessels, but no statistical reports have been found in the literature.

From these studies and investigations it is obvious that the situation is more serious than it appears on casual observation. The chronic ailments with their disabilities and deaths resulting from the remote effects of slow gassing must be reckoned with in order properly to evaluate the full significance of the hazard.

Increased Incidence of Encephalopathies in Victims of Slow Carbon Monoxide Asphyxiation

Hospital *	Admissions	Encephalitis	Epilepsy	Tetany	Multiple Sclerosis	Ratio of Admissions
Union Memorial..	83,685	48	...	..	..	1:1,819
			101	..	..	1:828
				4	..	1:20,921
					24	1:3,487
Mercy.....	41,415	40	...	..	..	1:1,035
			106	..	..	1:391
				1	..	1:41,415
					9	1:4,602
Diagnostic Clinic†	8,112	41	...	..	..	1:198
			55	..	..	1:148
				6	..	1:1,352
					6	1:1,352
Carbon monoxide group	150	13	...	..	..	1:12
			9	..	..	1:17
				2	..	1:75
					3	1:50

* Both Union Memorial and Mercy Hospitals admit all classes of patients. In the Diagnostic Clinic the patients admitted are chiefly those with medical conditions, most of which are of a chronic nature.
† Exclusive of carbon monoxide cases.

Our studies emphasize the fact that the carbon monoxide problem in the state of West Virginia is quite different from that in the state of Maryland. In the former it appears to be largely domestic, in the latter it is obviously more industrial. As a domestic problem, removal of the danger is fraught with greater difficulty. The best results could be obtained by a campaign of education followed by strict enforcement of laws regulating sanitary and environmental hygiene. This will require thorough organization and complete cooperation between the state board of health, the general medical profession and the lay public. The task confronting those dealing with the problem of carbon monoxide as an industrial hazard is less difficult, as laws have already been enacted which can be better enforced through well organized business groups where the health of the employees becomes a major economic factor.

In order fully to appreciate the manner in which the tissues react to carbon monoxide in producing symptoms of the so-called chronic or delayed forms and residual syndromes of acute carbon monoxide anoxemia, it will be necessary to restate briefly its mode of action when inhaled and the pathologic lesions which result in consequence.

Although carbon monoxide is considered chemically nontoxic, yet when inhaled in sufficient amount it produces a characteristic train of symptoms, the severity and chronicity of which depend on the degree of atmospheric concentration, the frequency and duration of exposure, the temperature and humidity of the air, the amount of physical exercise and the general health and susceptibility of the individual.

While concentrations of 0.01 per cent or less do not give rise to any symptoms, a concentration of 0.02 per cent will cause mild symptoms after several hours' exposure. Thus the safety limit for continuous exposure of industrial workers has been established by health authorities at a concentration level of 0.01 per cent.

The effect of carbon monoxide on the health of an individual is due mainly to the replacement of oxygen, which normally combines with the hemoglobin of the blood, by carbon monoxide, for which hemoglobin has a much greater affinity.

When the blood becomes saturated with carbon monoxide to a degree of 25 or 35 per cent the individual suffers from oxygen deprivation and a state of anoxemia exists. Accordingly, the symptoms of carbon monoxide asphyxiation are primarily those of anoxemia and are similar to those occurring in any other state of anoxemia. Symptoms quite different in character may develop later as secondary manifestations caused by organic tissue changes, the result of severe or persistent anoxemia. These frequently appear as sequelae after partial or even complete symptomatic recovery from acute asphyxia, or after repeated exposure to fluctuating amounts of the gas over prolonged periods.

PATHOLOGIC ANATOMY

There is a remarkable unanimity of opinion with respect to the character and distribution of the pathologic lesions produced by carbon monoxide asphyxiation as witnessed at autopsy by many observers, both in patients and in experimental animals.

Briefly stated, these lesions are fundamentally vascular and may affect any organ. The organs sustaining the greatest damage are those endowed with the richest blood supply, notably the brain and the heart. The pathologic changes consist of dilatation of the peripheral vessels, slowing of the blood stream and increased permeability of the vessel walls, with tendency to hemorrhage, perivascular infiltration and edema.

Although hemorrhages occur most frequently in the capillaries and the smaller vessels and are generally minute, petechial in form and well disseminated, they also occur in larger vessels and in rare instances have caused death.

Coronary thrombosis has repeatedly been observed clinically and at autopsy as well as in experimental animals in states of carbon monoxide anoxemia. The associated lesions of infarction and softening lead to cardiac dilatation, congestion, heart failure and death. Dyspnea, palpitation, cough and precordial pain were among the leading cardiorespiratory symptoms.

On the same underlying pathologic basis, cerebral syndromes develop. Predominant among these is a form of hemorrhagic encephalitis which occurred in 8.6 per cent of our cases. Other lesions of the central nervous system were manifested by symptoms of multiple sclerosis, hemiplegia, tetany, epileptiform seizures, syncopal attacks, emotional episodes, visual disturbances

and various forms of neuroses and psychoses, some with marked mental deterioration.

In the digestive tract were noted such symptoms as glossitis, perversion of taste, cardiospasm, pylorospasm, enterospasm, anorexia, nausea, vomiting and epigastric pain; the latter symptoms were often associated with food ease and hunger pain, simulating ulcer. Many patients suffered from spastic constipation.

In the urogenital domain nocturia, dysuria, albuminuria and glycosuria were the most outstanding features. Functional menstrual disorders in the female and impotence in the male were common symptoms.

Owing to the widespread lesions of the secondary forms of carbon monoxide anoxemia, the symptoms are too varied and bizarre to be presented in the form of a definite clinical picture. The fact is that the symptomatology is representative of multiple syndromes and can be correlated with those caused by similar vascular lesions from other sources affecting the different organs or systems. For a more complete discussion of the clinical aspects of the subject, recourse may be had to our previously published articles.

The following cases, some of which have been previously reported, are cited to illustrate certain clinical forms of slow carbon monoxide asphyxiation:

REPORT OF CASES

CASES 1 and 2.—*History.*—Mr. G. P., a meat cutter aged 25 years, and his wife, aged 23 years, of West Virginia, referred by Dr. Sisler for study and diagnosis, complained chiefly of symptoms from which they suffered in common consisting of headache, weakness, vertigo, neuromuscular pains (shoulder, back and extremities), muscular twitchings, cramps in the toes, numbness and tremor in the legs, staggering gait, cough, anorexia and nausea.

They were both overweight and they both had an abnormally low blood pressure and infected tonsils. All laboratory tests were negative except in the case of Mr. P., who had a red cell count of 5,112,000 with a hemoglobin content of 90 per cent.

The morning they arrived at the clinic it was noted that they both had difficulty in walking. Their gait was slow, hesitating and staggering. The following day there was marked improvement, and the fourth day, on leaving the clinic, they walked perfectly normally. According to their own statement, the headache, neuromuscular pains and weakness in the legs had disappeared and they walked 100 per cent better.

Carbon Monoxide History.—Natural gas was used throughout the house for heating and cooking. There were no open fireplaces and there was no attempt at ventilation. On cold nights they slept with the gas burning in their bedroom. They usually woke up in the morning with headache, which passed off when they got into the open air. The odor of gas was frequently noticed. Their 3 year old boy slept in a room with gas burning and windows closed. He was sickly, pale, too weak to play and vomited every two or three days. The year old baby slept in the room with the parents. It was puny, weak, sickly, pale and suffered with vomiting and diarrhea. Five canaries were kept in an adjoining room heated with gas and unventilated. With the onset of cold weather the birds quit singing, refused food, became weak and shaggy and died one after the other.

A year later Dr. Sisler wrote that after the source of carbon monoxide was removed there was no return of symptoms, and that the children were healthy, robust and had splendid appetites.

This family group represents the simple uncomplicated form of carbon monoxide anoxemia in contradistinction to the more chronic forms exhibiting residual symptoms. This is indicated by the prompt subsidence of all symptoms when the inspired air was freed from the gas and by the subsequent history, which showed that the family escaped the more serious and permanent after-effects characteristic of the chronic forms. The canaries, which succumb to its effects more readily than human beings, died from slow asphyxiation, and as children, and especially young infants, succumb more readily than adults, it is surprising that they survived. Before suitable chemical tests were available for the detection of dangerous amounts of carbon monoxide gas, canaries were sacrificed for the purpose. Who knows how many infants may have been sacrificed innocently?

CASE 3.—Mr. A. C., a restaurateur aged 29 years, from West Virginia, referred by Dr. Sisler, complained of conditions which corresponded very closely to those described by Mr. and Mrs. P. The outstanding symptoms were weakness, headache, vertigo, nausea, vomiting, dysphagia, ataxia, cough, dyspnea, myalgia, muscular twitchings and stiff and painful joints.

The physical examination was negative except for obesity and absence of patellar reflexes. The blood showed 100 per cent hemoglobin, 7,830,000 erythrocytes and 10,200 leukocytes, with a normal differential count.

For three years he had worked on an average of sixteen hours a day cooking over a gas stove in a restaurant, which was also heated by gas stoves. He also burned gas in the home and, during the winter months, slept with the gas burning in his room. At the restaurant he could often detect the odor of gas, to which he attributed his headache, vertigo, nausea and difficulty in swallowing. He was unable to get relief from these symptoms unless he went outdoors into the open air.

The most interesting feature in this case is the polycythemia, which has considerable diagnostic value. Thirty-six per cent of our patients had a red cell count of over 5,000,000. Davis, who studied the blood of 174 men employed at a blast furnace, found 64 per cent with a red cell count over 5,000,000.

Nasmith and Harrison, by subjecting rabbits and guinea pigs to a carbon monoxide blood saturation of 25 per cent, noted after the third day a steady rise of the erythrocytes until a maximum was reached in three or four weeks, after which the count remained constant. The hemoglobin is also increased but not in the same proportion. In our series it exceeded 100 per cent in nineteen cases. With the exception of occasional leukocytosis no significant changes have been observed in the white cells.

Ten per cent of our cases were associated with various grades of anemia, in which the red cell count was below 4,000,000 and the hemoglobin below 78 per cent. Three of the cases presented a typical picture of pernicious anemia, of which the following two are examples:

CASES 4 and 5.—Mr. and Mrs. C. (husband and wife) of West Virginia, both aged 62, were admitted to Mercy Hospital with symptoms characteristic of advanced addisonian anemia. The onset, duration, clinical course, symptomatology and objective features were singularly identical in the two patients. The husband's blood showed 60 per cent hemoglobin and 1,766,000 red cells, and the wife's showed 64 per cent hemoglobin and 1,936,000 red cells. Both had gastric achylia and complained of sore tongue, profound weakness, paresthesia, headache, vertigo, stupor, palpitation and dyspnea. The wife recovered after several transfusions and with improved heating conditions. Her hemoglobin rose to 80 per cent and the red cell count to 4,064,000. The husband died despite transfusions.

A common etiologic factor was suspected because of the nature of the illnesses, which seemed strikingly similar in every detail in the husband and wife. On careful inquiry it was ascertained that for eighteen years the family burned gas from their own well for cooking and in open unvented stoves for heating. During the winter months gas was burned continuously day and night in the rooms occupied by the patients without

adequate ventilation. The children, who slept on the second floor without gas heat and with wide open windows, remained healthy. Their dog, which was allowed to occupy the same quarters as the patients, where he spent much of his time sleeping in front of an open fire, was taken ill. He ceased to romp and play, refused food, became weak, sluggish and drowsy and dragged his hind legs when he attempted to walk. He died from the effects of gas in December.

It is doubtful whether or not carbon monoxide alone is responsible for the associated simple or aplastic forms of anemia occasionally occurring in the course of slow asphyxiation. It may possibly be due to an admixture of other gases or vapors contained in natural or illuminating gas. In this particular instance the family burned the unrefined "raw" or "wet" gas from an adjacent well. These unrefined gases are known to contain certain products which have a deleterious effect on the red blood cells.

The nature and severity of the delayed or secondary symptoms seem to vary in different localities. For example, in Ritchie County, W. Va., where there are extensive gas fields and much gas is consumed for domestic purposes in its raw state, lesions of the central nervous system and the heart are very common. Workmen engaged in cleaning and repairing gas wells are particularly susceptible to angina pectoris and organic heart disease. This observation suggests an additional causal factor to that of carbon monoxide attributable to the toxic volatile vapors (pentane, hexane, heptane, octane) which are constituents of natural gas. These are known to produce lesions with symptoms similar to those of carbon monoxide anoxemia. They differ, however, in their effect on the blood, in which there is a tendency to anemia instead of polycythemia.

In order to provide a cross section illustrating the various clinical types of disease resulting from prolonged exposure to the gas, all the patients studied from Ritchie County will be included in the following case reports.

Among this group there were two cases each of encephalitis, tetany and epilepsy and one each of emotional episodes and syncopal attacks. One of the cases of encephalitis was associated with tetany and hypopituitarism and one with coronary thrombosis. There were five cases of angina pectoris, one of which was associated with tetany, and two cases of coronary thrombosis, one associated with encephalitis and one with angina pectoris. A case of carbon monoxide anoxemia was complicated by hypothyroidism. A patient with chronic bronchitis was suspected of having tuberculosis.

CASE 6.—Mrs. G. G., aged 25 years, a housewife of Pennsboro, W. Va., gave a history of living in gas-heated rooms for the past twenty years. In recent years she also cooked with gas and slept in a room heated with gas. For the past two years she had been very ill, suffering with vertigo, nausea, daily vomiting, epigastric pain and constipation alternating with diarrhea. Since the onset of illness she had been subject to periodic attacks of what she described as "queer" spells. These occurred at irregular intervals and usually lasted for about half an hour. During these attacks she would lie in a semicomatose state, without muscular spasms but with involuntary bowel movements. These attacks were invariably superinduced by exposure to gas and fluctuated in intensity according to the amount of exposure. She was free during the summer months, when she was not exposed.

After a period of rest, change of environment and improved heating conditions in the home, the vomiting and nervous attacks promptly subsided, her general health improved and she gained 35 pounds (16 Kg.).

CASE 7.—H. A. A., a boy aged 18 years, of Cairo, W. Va., complained of nervousness and gave a history of epilepsy. The first epileptic seizure occurred in November 1935. He had six subsequent attacks prior to examination in May 1936. In February 1936 he discontinued school on account of them. They were characterized by sudden onset, with transient loss of consciousness and clonic spasm of the muscles of the extremities during which he would occasionally bite his tongue. After the attack he would be mentally confused for a short period. The patient's house was heated by burning natural gas in radiant heaters, which were unvented. Gas was burned almost continuously in the room he occupied eight or nine hours daily. The following characteristic symptoms were attributed to the gas: headache, vertigo, drowsiness, yawning, dyspnea, palpitation, vomiting and muscular twitchings.

Physical examination showed a normally developed individual of asthenic habitus with a blood pressure of 138 systolic and 82 diastolic. He exhibited marked vasomotor disturbances as evidenced by local sweating, abnormal flushing, turgescence of veins and dermographism. The only abnormal neurologic features were absence of the abdominal and cremasteric reflexes on the right side. The blood showed a hemoglobin content of 97 per cent and a red cell count of 5,230,000, with a normal white cell and differential count. All other tests including the Wassermann were negative.

The patient had one seizure shortly after entering the clinic. He was instructed to improve the heating condition in the home, eat a well balanced nutritious diet and lead a regular hygienic outdoor life.

On December 5, eight months later, his father wrote: "H. has not had a nervous attack since he came home from Baltimore last May. He has gained 23 pounds (10 Kg.) in weight and is heavier than he has ever been. He is strong and vigorous and seems to be as well as he ever was. He takes lots of outdoor exercise such as baseball, long walks and tennis. We are taking every precaution to see that his room is well ventilated and that there are no fumes in it."

CASE 8.—V. M., a mill worker aged 22 years, of Mole Hill, W. Va., had been subject to epileptic seizures from the age of 12 years. There was no history of epilepsy in the family. He was exposed to gas, which was used in the home for fuel from his childhood. On account of his illness he was closely confined to his home. His mother, who was also closely confined, was suffering from symptoms of anoxemia. His health was good before the onset of the present illness. Until a year previously all the attacks were mild in character and occurred mostly at night, averaging from one to four in number. Since then he had had occasional major attacks. In these attacks he lost consciousness momentarily but never fell. He suffered from dull headache, vertigo, cardiospasm, cramps in the toes, insomnia and constipation, and he frequently became depressed and was highly emotional.

Results of the physical examination and the laboratory studies were essentially negative.

Numerous cases of epilepsy following slow carbon monoxide asphyxiation have been reported. It is also known that gasoline, a constituent of natural gas, as well as benzene may produce epileptiform convulsions; the fact that eight of the nine epileptic patients in this series reside in West Virginia, where natural gas is the chief source of fuel, suggests these volatile constituents as contributory factors. This applies more especially where wet or unrefined gas is used for heating and cooking, since wet gas contains more than three times the amount of gasoline found in dry gas.

These constituents have a somewhat similar effect to that of carbon monoxide in producing lesions, especially of the brain and central nervous system. This may explain why most of the patients residing in Ritchie County suffer from severe organic disease of the central nervous system as compared with those who came under our observation from Morgantown. In the former locality, analysis by the West Virginia Geological Sur-

vey of gas from the wells in the community showed a very much higher percentage of gasoline fractions than the gas from wells in the vicinity of Morgantown, where in some instances little more than traces were found.

Among the rare complications of carbon monoxide anoxemia is tetany, of which the following two cases are examples:

CASE 9.—Mrs. J. W., aged 51, a housewife from Pennsboro, W. Va., complained of peculiar nervous and cardiac attacks. Her daughter, 21 years old, had suffered from convulsions for the past three years. A year previously the patient began to suffer from vertigo and a staggering gait and for the past six months had had paroxysmal pain about the heart, associated with numbness and dull pain in the left arm. She frequently noticed palpitation and cardiac irregularity besides periodic muscular twitchings and spasmodic contractions of the toes and left thumb.

Gas was used for cooking and heating. She slept with a gas stove burning in her bedroom, but as it was defective and gave off "fumes" she would not allow it to burn continuously. Her greatest difficulty was in walking when she first got up in the morning. Among outstanding symptoms were peculiar attacks during which she felt nervous and exhausted and suffered from headache, vertigo and weakness in the legs. These were accompanied by belching and a feeling of discomfort about the heart. In her own words, she felt dazed and like her heart was being squeezed. After her first attack she became emotional, was unable to sleep and cried night and day. In the more severe attacks she had transient loss of consciousness, with considerable jerking of the muscles. Later the attacks became somewhat milder but increased in frequency to as many as six in a single night. All of them were accompanied by typical tetanic spasm affecting both hands and arms, associated with numbness and pain which lasted from ten to fifteen minutes. She could not recollect having had a single attack except during periods when she was burning gas.

On admission to the clinic, examination showed the patient to be somewhat underweight with a sallow skin and marked dermographia. There were puffiness about the eyes, drooping of the upper lids and injection of the conjunctivas. Except for an occasional extrasystole the heart was normal, and the blood pressure, pulse and temperature were normal. There was muscular hypertonicity, especially of the abdominal muscles, and considerable tenderness was present over both shins. All reflexes were hyperactive. A striking feature was the prompt cessation of the tetanic spasms and heart attacks as well as the headache, vertigo and ataxia, all of which disappeared within three days. The laboratory reports were negative throughout. By changing her heating system she continued to improve. A year later she wrote that she had not had any attacks, that her weight had increased from 109 to 145 pounds (from 49 to 66 Kg.) and, though she had occasional feeling of numbness in the hands and arms, that there had been no muscular spasms.

CASE 10.—Mrs. G. P., aged 27, a housewife from Pennsboro, W. Va., presented symptoms of chronic encephalitis, chronic tetany and hypopituitarism.

Four years before she began to complain of attacks of transient numbness in the left forearm and hand, lasting not over a minute. They continued at intervals, without changing in character or frequency, for three years, after which they increased in frequency and severity. They occurred usually at night, during which she would have two or three attacks associated with outcries but unaccompanied with pain. Later, in December, when in her sixth month of pregnancy, the nocturnal attacks increased in frequency from six to twelve each night and also in severity, being accompanied by severe pain and tonic contractions of the muscles of the left forearm and hand, forming the typical obstetric hand characteristic of tetany.

For two weeks prior to the delivery of her child she was confined to bed, mentally confused and disoriented and in a state of profound stupor from which she could not be easily aroused. During this period of illness the family noticed that there was gas escaping in the room, which was heated by a gas heater without a connecting flue. Her nurse became ill from the gas the first night on duty and suffered with nausea, vomiting, headache, vertigo and drowsiness. The patient's mother, who nursed her the next night, was also taken ill with nausea, headache and vertigo. The husband, who took the mother's place, spent less time in the room, but he, too, felt ill and suffered from headache, vertigo and loss of appetite. At the end of the week the heating system was changed, and the patient gradually emerged from the stupor with a return of her tetany attacks. However, during the summer months, from July to October, there was a marked diminution in their frequency.

Examination showed a hypopituitary type of individual, 30 pounds (14 Kg.) over the ideal calculated weight, with characteristic fat distribution, infected tonsils, marked vasomotor disturbances, slightly nodular thyroid, drooping eyelids, mydriasis and normal eyegrounds. There was tenderness over the insertion of the masseter muscles; hypertonicity of the skeletal muscles and hyperactive tendon reflexes were present.

Laboratory studies showed a serum calcium level of 9.1 mg., blood sugar 93 mg. and blood cholesterol 174 mg. per hundred cubic centimeters. The blood count, blood urea and urea nitrogen were normal and the Wassermann reaction was negative. There was gastric hyperacidity with slight six hour retention. The basal metabolic rate was —8 per cent, and the spinal fluid was normal. During the spinal puncture a typical attack of tetany developed.

A neurologic examination was made by Dr. Charles Bagley, who stated as his impression that she was suffering either from neoplasm in the right posterior central area or from encephalitis. The former has been practically excluded by the subsequent course of the disease.

Tetany appears to be a rare complication of carbon monoxide asphyxiation, as comparatively few cases have been reported. Therefore it is a rather remarkable coincidence that the only two cases which occurred in our series are included in this small group from Ritchie County. Tetany and epilepsy occasionally occur together in the same person; epilepsy has occurred as a sequel in encephalitis. Epilepsy when associated with encephalitis is due to brain injury especially involving the cortex. Tetany cannot be accounted for in the same manner; it is probably due to the effect of gas on the endocrine glands, especially the parathyroids.

CASE 11.—Mr. G. D., aged 36, a farmer and cattle dealer from Pike, W. Va., referred by Dr. Jones and Dr. Woodyard, presented a history of coronary thrombosis, heart block and symptoms of encephalitis with parkinsonian syndrome.

The mother died of angina pectoris and the father of paralysis agitans. The family lived in the midst of a newly developed oil and gas field, and at the time of the patient's illness there were twenty-nine wells located within a radius of a mile from his residence. For a time the wells were allowed to "flow open." The gaseous vapor of some of these wells was piped up on a hill away from the road, to which it would drift and make traffic dangerous and at times almost impossible. His house was heated day and night by burning the unrefined wet gas in open unventilated heaters. The heater in his bedroom was defective and an odor of gas was detected, for which the doctor ordered better ventilation. When the patient was taken sick in February 1935 with symptoms suggesting influenza, he was confined to this room. He had a temperature of 103 F. He was stuporous, delirious, gasped for breath, broke out in cold perspiration and was nauseated and vomited. Both his wife and sister, who were in attendance, became ill from the gas and suffered from nervousness, headache and vertigo. The patient was later referred to the hospital, where a diagnosis of coronary thrombosis was made. In June, following extraction of teeth, heart block developed, with a pulse rate of 30 per minute and the typical Adams-Stokes syndrome. This condition slowly subsided but he continued to be nervous, emotional and obsessed with fear.

On admission to the clinic Sept. 25, 1935, he was in a highly emotional state, introspective and afraid to be left alone. He was considerably overweight and exhibited the characteristic

features of the parkinsonian syndrome, including the masklike expression, flushed face, dry, desquamating skin, muscular rigidity and inability to feed himself, sit erect or stand and walk unaided. His speech was slow, hesitating and monotonous. The blood pressure and heart measurements were normal. There were occasional extrasystoles associated with a soft systolic murmur at the base. The abdominal reflexes were absent, the plantar reflexes were normal and the deep tendon reflexes were hyperactive. There was marked motor weakness with tremor of the tongue and both hands. The neurologic diagnosis of chronic encephalitis, probably the result of chronic carbon monoxide anoxemia, was confirmed by Dr. Gillis.

Dr. King, who saw him later in consultation, found his heart normal on physical examination except for extrasystoles, and the electrocardiogram was negative except for the extrasystoles.

The only positive laboratory evidence consisted of an occasional trace of sugar in the urine, a red cell count of 5,620,000, a hemoglobin content of 100 per cent, and leukocytosis with 13,000 cells and a normal differential count. The basal metabolic rate was —8.6 per cent.

CASE 12.—Mrs. Z. B. M., aged 48 years, a school teacher from Mole Hill, W. Va., had been living for the past twenty years in a home heated by burning natural gas in open unvented gas heaters. Besides, she had been exposed in her school room, in which she taught for eleven consecutive terms. This room was heated in a similar manner. In both home and school room, gaseous odors could often be detected. As a result of her exposure she suffered not only from a severe form of carbon monoxide anoxemia but also from hypothyroidism, a condition often associated with chronic anoxemia. As a symptom of the latter, severe intolerance to cold developed. In order to sleep, she burned gas in her bedroom at night and resorted to the use of extra heavy blankets. Our clinic records show that on the night of July 1 she slept under two sets of blankets with a hot water bottle.

Although the patient had suffered for many years from headache and nervous symptoms, her condition became progressively worse after an attack during which she had, among many other symptoms, severe headache, nausea, vomiting and diplopia. Since then she had continued to suffer with terrific headache, severe vertigo, weakness, staggering gait with a tendency to fall, cramps in the muscles in the legs and hands, twitching muscles of the face and paresthesia of the arms and legs. Her friends noticed a striking change in her personality.

There were twelve members of the family, all of whom lived in the same home environment and all of whom suffered during the winter months from severe headaches and many of the other symptoms enumerated. They all, including the patient, felt better in the summer than in the winter.

A group of symptoms were referable to thyroid deficiency. These include drowsiness, sighing, retarded memory, lack of concentration, tinnitus aurium, muscae volitantes, visual hallucinations of seeing animate objects passing, auditory hallucinations of hearing her name called and bells ring, intolerance to cold, dry skin, brittle nails and snapping joints.

After two weeks in the clinic it was noted that symptoms referable to carbon monoxide anoxemia, namely headache, vertigo, ataxia, muscular cramps and fibrillations and paresthesia, had practically all subsided, while those of hypothyroidism were still persisting although they were greatly ameliorated.

In both anoxemia and hypothyroidism the clinical manifestations are almost entirely subjective. The only objective features in the case just presented were a slight degree of facial asymmetry with a tendency of the mouth to deviate to the left, a faint tremor of the tongue, dry skin and brittle nails, scanty axillary and pubic hair, genital hypoplasia, hyperactive tendon reflexes and absence of abdominal reflexes.

The urologic examination showed a chronic form of cystitis and trigonitis. All laboratory reports were negative except that of the basal metabolism rate, which was —19.2 per cent.

The basal metabolism is uniformly low in carbon monoxide anoxemia. In seventy-five cases in which the test was made there was only one (a case of toxic goiter) in which the rate was above normal. In sixty-five cases it was 0 or below, and in forty-four cases it ranged from —10 to —40. The tremor, facial asymmetry and absence of abdominal reflexes suggest the possibility of a mild chronic form of encephalitis. The latter is a frequent complication of carbon monoxide gassing.

CASE 13.—Mr. L. J., aged 55, suffered during the winter months with a severe intractable bronchial cough and symptoms characteristic of anoxemia. On account of these symptoms and the persistence of the cough, tuberculosis was suspected.

He gave a history of overexposure to gas in his office, heated by open heaters, where he spent many hours during the day. Since gas was suspected as a possible cause, examination was deferred three days. By that time the cough as well as all other symptoms had subsided, and the physical examination was negative for tuberculosis. After reconditioning his heating system he remained free from symptoms.

CASE 14.—Mr. S. M. C., aged 55, manager of a tourist camp in Ellenboro, W. Va., complained of acute paroxysmal pain in the left side of the chest, irregular heart and shortness of breath. His father had heart trouble and a brother suffered from angina pectoris.

Seven years previously he began to suffer with palpitation and rapid pulse. He felt nervous and was heart conscious, but no organic disease of the heart was found on examination. Two years previously his heart symptoms became more pronounced. He noticed some intermission of beats with rapid heart action and a pulse rate occasionally as high as 120 per minute. At the same time he began to complain of pain about the heart on exertion such as going up hill, when typical attacks of angina pectoris developed.

Among other symptoms were headache, weakness, vertigo, blurring of vision, neuromuscular pains, cramps in the toes, paresthesia, impotence, constipation, hemorrhoids and dysuria.

Examination showed the heart slightly enlarged, normal in rhythm and free from murmurs. The blood pressure and pulse rate were normal. The prostate was somewhat enlarged. Results of laboratory studies were negative throughout.

The patient heated his house with natural gas supplied from his own wells, which he burned in the "wet," unrefined state. There were nine open heaters in the house. On cold winter nights he slept in a room with the gas burning. Carbon monoxide tests indicated dangerous amounts of gas in some of the rooms occupied. After he was freed from exposure to gas by installation of a central heating plant, his health improved. On examination a year later he stated that he felt better than he had felt for years and that although he had been physically active he had been entirely free from attacks of angina pectoris. A strenuous two days hunting trip in the mountains failed to bring on an attack.

On his last examination, Oct. 10, 1939, he had no recurrence of angina pectoris, his heart was regular and free from murmurs, the electrocardiogram was normal and his general health was excellent.

CASE 15.—Mr. W. L. B., aged 62, from Pennsboro, W. Va., was admitted to the clinic Oct. 16, 1939, complaining of severe paroxysmal pains in his chest. Since 1911 he had been engaged in repairing and cleaning oil and gas wells. He was subjected to the gas and vapors escaping from these wells daily, year in and year out. Both he and his co-workers frequently suffered from nausea, weakness and tremors while at work. These symptoms were always ameliorated by inhaling fresh air. The patient was also exposed to gases in the home, which was heated by radiant heaters, unvented. The odor of gas could frequently be detected.

In January 1938 he began to suffer with dyspnea on exertion. In June there developed attacks of paroxysmal precordial pain which radiated down both arms. The first attack occurred after overexertion while he was working on a well from which much gas escaped. Subsequently he had averaged one attack

about every two weeks. Amyl nitrite promptly relieved the pain, but morphine sulfate gave only partial relief.

In February 1939, while sleeping in a room heated by a gas stove, he contracted headache, vertigo, nausea, dyspnea, weakness, sweating and paresthesia. Since then he had had slight ataxia with muscular soreness, fibrillations and cramps. He had been constipated for the past year and his stools were spastic in character. The physical examination was generally negative. The heart was regular; the sounds were distant; no murmurs were heard. The blood pressure, pulse and temperature were normal. Results of laboratory studies likewise were negative with the exception of the blood, which showed a hemoglobin of 94 per cent, 6,140,000 red cells and 7,000 white cells with a normal differential count. Electrocardiographic studies showed progressive changes in Q_3, T_3 and QRS_2, suggesting occlusion of the right coronary artery with damage to the posterior base of the left ventricle.

CASE 16.—Mr. J. G., aged 45 years, from Greenwood, W. Va., worked for years in Ritchie County as a gas well driller and later in a machine shop where he was also exposed to gas. As a child he was healthy except for occasional attacks of tonsillitis and an attack of rheumatism at the age of 20. Three years later he passed the examination for the army, and he spent a year in active service abroad during the World War. The following year a heart lesion was detected but he continued to work until 1927, when he became disabled. His chief symptoms were dyspnea and palpitation. Recently angina pectoris developed, with an average of about one attack every four or five days. It usually occurred on exertion, especially when he was facing cold winds.

The attacks were more frequent in winter, when he spent much of his time in the house in front of an open gas fire. He could recall having had only three attacks during the summer months.

The chief symptoms referable to carbon monoxide anoxemia were headache, vertigo, weakness, neuromuscular pain, fears and anxieties, paresthesia, fibrillating muscles, cramps in the legs and toes, tremors and yawning. On his arrival at the clinic Jan. 10, 1938, the blood showed a carbon monoxide saturation of 18 per cent.

His house was heated with six open stoves, three radiant heaters and three old-fashioned burners, none properly vented. His wife, who was similarly exposed, suffered the same symptoms except that she was free from angina pectoris. The daughter, who taught school and spent less time in the house, remained well.

Examination of the heart showed some enlargement and the characteristic physical signs of mitral stenosis, although the electrocardiogram did not show anything strikingly abnormal.

Laboratory examinations were generally negative.

CASE 17.—Mr. C. E., aged 47 years, from Greenwood, W. Va., complained of shortness of breath and acute heart attacks.

With the exception of twenty-one months while serving in the army, he was daily exposed to gas over a period of twenty-two years in his occupation of drilling and cleaning oil and gas wells in Ritchie County. He was also exposed from the age of 12 years in his home, which was heated by burning raw gas in open heaters. His wife and son both suffered from the effects of the gas, and his brother, 48 years old, who also burned unrefined gas in the home, died suddenly from a heart attack while at work in the same gas and oil fields.

The patient's health was good until a year previously, when he first noticed heart symptoms such as paroxysmal precordial pain, fluttering sensations about the heart and dyspnea on exertion. He progressively got worse until Jan. 3, 1938, when he was no longer able to work. A week later, when he entered the clinic, the blood showed a carbon monoxide saturation of 25 per cent. On the train en route to the clinic he had several typical attacks of angina pectoris. Three weeks before, while eating supper in front of an open fire, he suddenly became blind and remained so for an hour. The symptoms characteristic of severe anoxemia included headache, vertigo, amnesia, confusion, ataxia, tremors, muscular twitchings, paresthesia, perverted taste, anorexia, intestinal cramps, weakness and impotence.

Nothing was found on physical examination to suggest any serious organic disease. The heart was normal in size, rate and rhythm. There was reduplication of the first sound but no murmurs. The electrocardiogram was normal. Laboratory studies showed gastric hyperacidity and a basal metabolic rate of —14.5 per cent. Otherwise the results were negative.

After a period of rest in a more wholesome atmosphere his health was restored, and by reconditioning his heating appliances in the home and exercising greater caution in preventing any unnecessary exposure to gas in his occupation, he has been able to work regularly without recurrence of symptoms.

COMMENT

As previously stated, the central nervous system and the heart sustain the greatest damage in carbon monoxide anoxemia. In the brain the area of predilection for the characteristic hemorrhagic lesions is in the basal ganglions, in which the corpus striatum is especially involved. The lesions in this area cause the clinical manifestations of encephalitis, of which there were thirteen cases in the series, most of them of the parkinsonian type.

In the heart there is also an area of predilection, confined largely to the left ventricle and the papillary muscle of the mitral valve. These hemorrhagic lesions are frequently found at autopsy in human beings or in experimental animals subjected to carbon monoxide.

It is interesting to note the frequency of symptoms of angina pectoris in this small group of cases from Ritchie County, especially among the men who had been working in the gas fields. The increase in the incidence among these workers leads one to suspect causal factors other than carbon monoxide. As previously stated, some of the constituents of "wet" gas, to which they were exposed, namely gasoline fractions, are poisonous and produce symptoms similar to those of carbon monoxide anoxemia. The fact would explain why the incidence of angina pectoris or other myocardial diseases associated with carbon monoxide asphyxiation occurs in a much smaller percentage of cases in Maryland or in districts where no natural gas is consumed.

There has been a prevailing opinion that unless carbon monoxide produces complete loss of consciousness no permanent injury ensues. The result of our investigation does not support this view, as there were only a few histories of loss of consciousness in the entire series. None of the patients suffering with symptoms of angina pectoris gave such a history. This observation is confirmed by Kroetz, who states that pain of an anginal character with typical radiation may appear if the inhalation of gas does not lead to unconsciousness.

The effects of carbon monoxide on the heart have been fully discussed in one of our previously published articles.[1]

There is still some question, especially in the minds of those engaged in laboratory research, as to the actual existence of the late or residual manifestations of carbon monoxide anoxemia, but in the minds of the internists and those engaged in industrial medicine there is less doubt. Two of our cases in which autopsy was recently performed support the view regarding the effect of carbon monoxide on the central nervous and cardiovascular systems:

The first was a case of acute poisoning in a woman 56 years of age who died forty-eight hours after the exposure. The brain showed numerous petechial hemorrhages scattered throughout with leukocytic infiltration, areas of focal necrosis and edema.

1. Beck, H. G., and Suter, G. M.: Role of Carbon Monoxide in the Causation of Myocardial Disease, J. A. M. A. **110:** 1982-1986 (June 11) 1938.

The heart also showed many areas of hemorrhage with focal necrosis, disruption and fragmentation of the muscle fibers.

In the other case a man aged 43, who for twenty years drove a taxicab, had recently suffered from typical carbon monoxide anoxemia as a result of exhaust gas from a leaking engine. Although he never lost consciousness he became incapacitated for work and finally, after many months, died from the effects of the gas.[2] The autopsy showed:

1. Generalized arteriosclerosis with marked sclerosis of the coronary and cerebral arteries.
2. Organizing and fresh thrombi of the basilar cerebral arteries.
3. Miliary cerebral infarction demonstrated in both cerebrum and cerebellum.
4. Cerebral edema.
5. Moderate cardiac hypertrophy with marked myocardial fibrosis and acute degeneration.

Only a few weeks before his death he was suspected of malingering.

Such evidence, combined with the characteristic clinical symptoms of carbon monoxide anoxemia coupled with a definite history of exposure to gas extending over a long period with relief from symptoms when not exposed, should afford ample proof that carbon monoxide may have a serious and damaging effect on the health, even without a history of severe acute asphyxiation or loss of consciousness.

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THE PRESENT STATUS OF THROMBOCYTOPENIC PURPURA

WITH SPECIAL REFERENCE TO DIAGNOSIS AND TREATMENT

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The exhibition of purpura as a clinical sign of disease was first ascribed solely to the effects of pestilential fevers. With the demonstration, however, by Denys[1] in 1887 that the purpura of Werlhof is characterized by a lowered level of circulating blood platelets, the clinical purpuric states were definitely shown to consist of thrombocytopenic and nonthrombocytopenic groups. Further differentiation within the thrombocytopenic group has been accomplished slowly since Denys's observations and has depended largely on cumulative experience with known etiologic states in which both purpura and marked thrombocytopenia have been observed to occur. There has thus arisen the practical and important subclassification of thrombocytopenic purpura into two groups—the idiopathic and the symptomatic. This is justified because the successful management of the former often requires life-saving surgery, whereas the latter should be managed strictly by medical means. The reversal of these therapeutic principles may promote disaster to the patient. The present discussion summarizes the current status of thrombocytopenic purpura of the idiopathic or essential type, with particular reference to diagnosis and treatment.

2. This case has been reported in detail (Beck, H. G.: Gastrointestinal Symptoms Simulating Ulcer in Chronic Carbon Monoxide Poisoning, Rev. Gastroenterol. **6**: 196-207 [May-June] 1939).

From the Department of Medicine, Ohio State University College of Medicine.

1. Denys, J.: Cellule **3**: 445, 1887.

PATHOGENESIS

1. *The Mechanism of the Bleeding Tendency.*—At present the only recognized hematologic abnormality which always occurs in this disease is a marked reduction in the circulating platelet level. Since the vital function of the blood platelet in the physiologic mechanism of blood clotting is well accepted, it would appear that the pathogenesis of bleeding is easily explained. Such, however, is not the case, for it has been occasionally observed that the platelets following the removal of the spleen in essential thrombocytopenic purpura may not be maintained at significantly higher levels and yet all clinical hemorrhagic manifestations disappear. Such atypical responses suggest a somewhat broader basic mechanism, namely (*a*) the platelet level in the blood may reflect or coincide, albeit imperfectly, with some other more fundamental disturbance in the tissues of the body on which blood coagulation depends and which is influenced by splenectomy (this view has again been championed recently by Tidy[2]), or (*b*) the bleeding tendency in this disease may be due to a combination of factors, of which the deficit in platelets is only one. Although it is always hazardous to speculate, it would seem that the second point of view is more likely to approximate the facts. Until there is a more satisfactory answer to such fundamental questions as to why the circulating blood remains fluid in the vascular system but coagulates promptly otherwise, the difficulties in understanding the exact mechanism of hemorrhage in every patient with purpuric manifestations become apparent. Obviously the precise role that the platelet plays in the pathogenesis of this disease must await the discovery of more facts that relate to the many other phases of the blood-coagulation problem.

Suggestions that the capillary bed may be at fault either because of increased permeability in addition to thrombocytopenia[3] or because of the inability of the capillaries to contract adequately[4] provide attractive possible explanations for the cause of bleeding but in this disease are not supported by convincing experimental data. There is very little doubt that a defective endothelial structure may result in bleeding, but that such defects are present in purpura haemorrhagica have not been demonstrated. Nevertheless, the vulnerability of the capillary vessels must be a very important circumstance in preventing the loss of platelets and other blood elements to the tissues. The fact that some persons will show petechiae with platelet counts of 100,000 or above, while others show no hemorrhage at platelet levels below 10,000, may be explained on this basis. The fact that the majority (not all) of the patients afflicted with this disease have a prolonged "bleeding time" has been cited as evidence of some obscure change in the capillary endothelium, but until all the factors which influence the mechanism of this test are known the significance of this observation must remain largely speculative.

No deficiencies in the soluble substances of the blood that have been found essential for blood coagulation can be demonstrated. The fact that the blood obtained in the active stages of this disease forms a clot that retracts either slowly or not at all is directly traceable to the paucity in platelet content. It is probably true that failure of the clot to retract and squeeze out serum results in a lack of firmness and impairs its value as a mechanical plug. This may be granted as a liability for

2. Tidy, H. L.: Brit. M. J. **1**: 583 (April 7) 1928.
3. Bedson, J. P.: J. Path. & Bact. **25**: 94 (Jan.) 1922.
4. MacKay, W.: Quart. J. Med. **24**: 285 (April) 1931.

effective hemostasis and may be of more importance in determining the bleeding tendency than is usually accorded the phenomenon.

2. The Mechanism of Thrombocytopenia.—(*a*) The Spleen: Kaznelson's designation of this disease as "thrombolytische purpura" descriptively presents what is now most widely held as the probable role played by the spleen in the pathogenesis of this disease. The belief that the spleen is chiefly responsible for the thrombocytopenia is due to two facts: (1) sternal marrow studies have consistently revealed normal numbers of normal appearing megakaryocytes in a normal cellular setting, and (2) splenectomy has been followed usually by the prompt reappearance of large numbers of platelets in the peripheral blood with a disappearance of all bleeding tendencies. Because it is difficult to demonstrate increased sequestration and phagocytosis of the platelets in the spleens removed from these

Comparative Bone Marrow Counts Before and After Splenectomy in Thrombocytopenic Purpura

Type of Cell	Before Operation*	After Operation†
	No. per Cu. Mm. "Marrow"	No. per Cu. Mm. "Marrow"
Total Counts		
All nucleated elements	211,875	153,857
Red blood cells	3,971,000	3,991,666
Megakaryocytes	152.4	137.8
W.B.C. : R.B.C. ratio	1.7:1	2.2:1
White Cell Elements	Per Cent	Per Cent
Neutrophilic leukocytes	31.9	31.0
Neutrophilic metamyelocytes	3.3	2.7
Neutrophilic myelocytes C	45.6	44.1
Neutrophilic myelocytes B	6.7	3.2
Neutrophilic myelocytes A	1.4	0.7
Eosinophilic leukocytes (all types)	4.2	8.3
Basophilic leukocytes (all types)	0.6	0.4
Myeloblasts	0.4	0.2
Small lymphocytes	2.5	2.8
Monocytes	0.4	0.7
Megakaryocytes	1.9	1.1
Red Cell Elements	R.B.C. per 200 W.B.C.	R.B.C. per 200 W.B.C.
Normoblasts	117.6	87.5
Erythroblasts (late)	27.8	33.2
Erythroblasts (early)	13.3	9.0
Megaloblasts	1.6	1.0
Tissue Cell Elements	Per Cent	Per Cent
Primitive cells	0.1	0.3
Clasmatocytes	0.9	4.0
Plasma cells	0.1	0.7

This table shows significant increases in levels of megakaryocytes and normoblasts in cases of essential thrombocytopenic purpura preoperatively as compared with the postoperative state. The white cells are not significantly altered, either in number or in type. The change in white blood cell–red blood cell ratio is obviously caused by the postoperative decrease in normoblastic units. It is believed that the increase of erythrogenic tissue before operation is satisfactorily explained on a basis of loss of blood occurring at that time.
* Eleven cases. † Six cases.

patients, owing chiefly to the physical characteristics and the rapidity of lysis of these elements, the exact manner in which the thrombocytopenia is brought about is not regarded as entirely settled. Our own experience with the supravital technic in assaying the specificity of the phagocytic activity of the splenic clasmatocytes as it relates to the various types of circulating blood elements has convinced us that this mechanism probably accounts for the thrombocytopenia under these circumstances. A possible analogy is seen in the mechanism of the production of anemia in congenital hemolytic icterus and in the recently discovered and described type of severe neutropenia due to excessive granulocyte phagocytosis by splenic clasmatocytes.[5] It is believed

5. Wiseman, B. K., and Doan, C. A.: A Newly Recognized Granulopenic Syndrome Caused by Excessive Splenic Leukolysis and Successfully Treated by Splenectomy, read before the Thirty-First Annual Meeting of the American Society for Clinical Investigation, Atlantic City, N. J., May 1, 1939; abstr., J. Clin. Investigation **18**: 473 (July) 1939.

that lysis of effete platelets is perhaps a normal physiologic function of the spleen. An augmentation of this function at times, until it has assumed pathologic proportions, appears most reasonable. Platelet counts

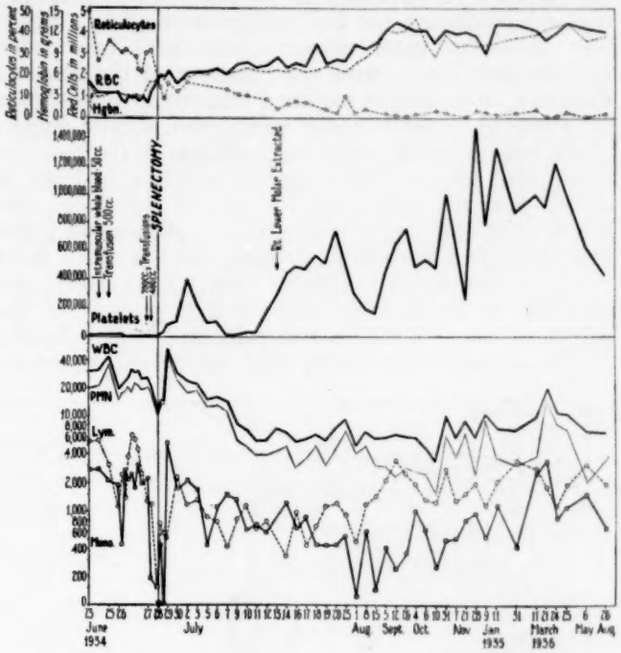

Chart 1 (E. M. R., a girl aged 17 years).—This case illustrates recovery after splenectomy from an acute type of thrombocytopenic purpura. Presenting massive hemorrhage at a platelet level of 3,500 and with red cells of 1,177,000, she was given a transfusion on June 25 without any diminution in the loss of blood. The platelets three days after admission were practically absent from the blood and the red cells had fallen to 800,000. Two transfusions (1,100 cc.) were given on the 27th and operation was decided on. A 110 Gm. spleen was removed the next day. In twenty-four hours the platelets numbered 89,000 with a steady rise to 748,000 by July 25. The secondary temporary dip in platelet level that followed is well shown on this chart and is a very common phenomenon. Charting is on a semilogarithmic scale.

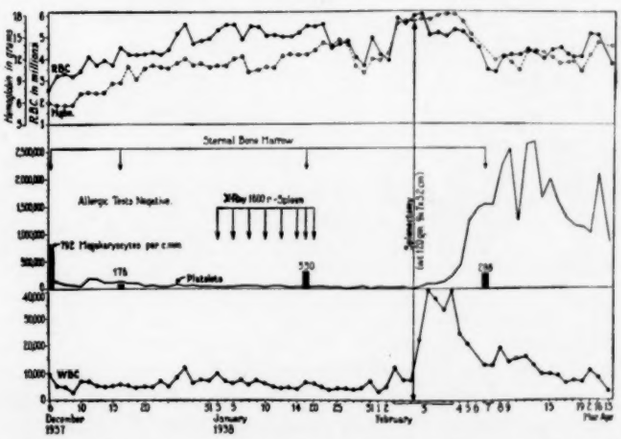

Chart 2 (L. S., a girl aged 14 years).—This case illustrates the actual development of marked depression of the blood platelets from 150,000 to 10,000 per cubic millimeter of blood while the patient was on an elimination diet regimen. After stabilizing at a level of about 10,000 platelets per cubic millimeter of blood for twelve days, she received high voltage roentgen therapy to the spleen on the days shown, each treatment in a dosage of 200 roentgens for a total of 1,600 roentgens. There was no effect on the platelet level or clinical state for the fourteen days following the last treatment. No favorable effect having appeared, splenectomy was accomplished with immediate rise in platelets shown on the chart. Charting is on a semilogarithmic scale.

obtained from the splenic artery and vein at operation have yielded inconstant results, but usually the platelet content of the venous blood has been definitely below that of the arterial blood. This has been true in our experience. The accuracy of this procedure in an organ

which sensitively contracts on manipulation, discharging its cellular contents into the vein in unpredictable amount, however, is more than doubtful.

There still remains to be explained the fact that, although the platelets may increase in numbers promptly and symptoms subside with the removal of the spleen, the values for these elements may later fall to the original low levels, with reappearance of the bleeding diathesis. It is usually assumed that either hypertrophy of accessory splenic tissue with clasmatocytic hyperplasia has occurred, or the macrophages of the reticuloendothelial system in other organs, such as the liver, in taking over the phagocytic function of the spleen also acquire the pathologic overactivity in destroying platelets. This is a reasonable explanation but again lacks adequate supporting evidence. Others have interpreted this fact as invalidating the entire hypothesis of the splenic etiology of the thrombocytopenia in this disease. Frank advanced the theory that the spleen depresses,

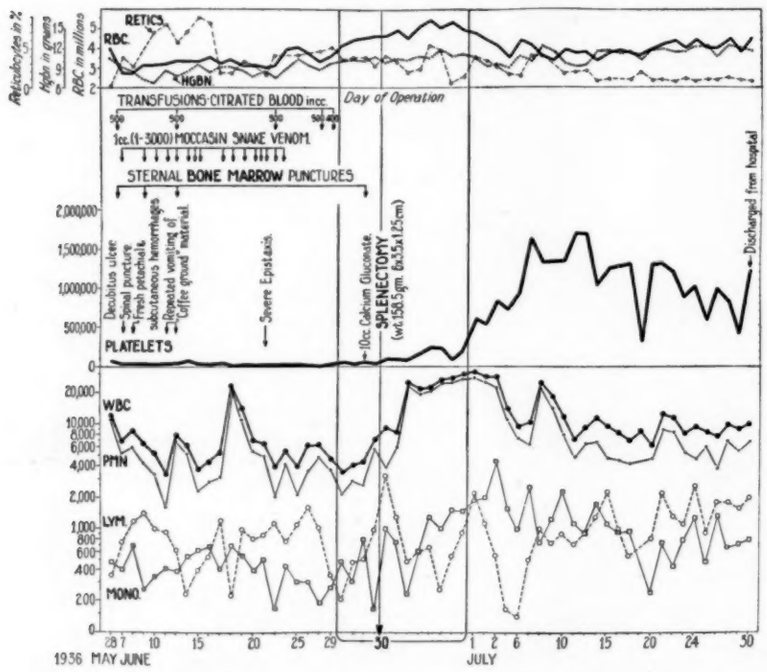

Chart 3 (A. J., a woman aged 61 with idiopathic purpura haemorrhagica).—This chart shows the absence of any rise in platelets after sixteen injections of moccasin snake venom in doses of 1 cc. each. Clinically, there was no diminution in bleeding. After splenectomy the usual rise in platelets immediately followed. The day of operation (June 30) is shown with twelve blood examinations taken at intervals to show the rapidity of rise in platelets after removal of the spleen.

by some as yet unknown method of remote hormone-like control, the megakaryocytes in the bone marrow so that they are functionally unable to supply adequate numbers of platelets. Although this hypothesis cannot be disproved at present, many students of the disease feel that the explanation afforded by the evidence for the theory of splenic cytolysis is much sounder. Troland and Lee [6] have recently reported that extracts of spleens removed from patients with thrombocytopenic purpura contain a substance ("thrombocytopen") which, when injected into the experimental animal, will depress the platelet levels. The attempted duplication of these experiments in our laboratory using monkeys and rabbits has so far failed to substantiate this work.

(*b*) The Bone Marrow: No evidence has yet been presented which demonstrates any intrinsic pathologic condition of the bone marrow. The megakaryocytes are either normal or more often increased in numbers, as shown in the accompanying table. Examination of these cells in the living state in supravital preparations has revealed no qualitative defects in our experience. Cannulization of the efferent vein is probably the only decisive method of determining the functional capacities of these marrow elements, but unfortunately this is not a practical procedure.

A mechanism which may result in peripheral thrombopenia has been suggested by the work of Madison and Squier.[7] Following their observations on the etiologic relationship between aminopyrine and malignant neutropenia, they noted that when patients with thrombocytopenic purpura were placed on elimination diets the blood platelets returned to normal levels. The fact that the megakaryocyte in some instances does become hypersensitive to specific allergens, particularly to drugs, cannot be doubted (chart 6). These cases should be regarded as symptomatic thrombocytopenic purpura. In our series of cases, tested by the method of Madison and Squier, there does not appear to be any relationship between the essential type of thrombocytopenic purpura as defined here and the allergic constitution.

PATHOLOGY

Widespread hemorrhage, both gross and microscopic, is the only constant feature found in this disease at necropsy. Most observers have found the bone marrow to be normal, which coincides with our experience. The spleen is usually normal and never more than slightly increased in size. Any case in which the spleen is easily palpated almost surely belongs to the symptomatic group of purpuras. The Nickerson and Sunderland series showed an average weight of 227 Gm. for six spleens removed surgically. The malpighian follicles were found to be enlarged and the germinal centers were active in all but two out of eleven specimens.[8] Our own studies on the spleens removed surgically have consistently failed to reveal any noteworthy gross abnormalities. The largest spleen in our series of surgical cases weighed 230 Gm., with an average of 124 Gm. We have found nothing noteworthy on study of the paraffin sections. Megakaryocytes are likely to be found in various tissues of the body including the spleen, probably an embolic phenomenon.

INCIDENCE

A study of the literature would indicate that this disease is more common in the female than in the male. In our series of twenty patients, fifteen were females. Approximately three of each five patients had this disease before the age of 21, and more than half before adolescence. It may occur, however, at any age and in any race. The disorder is often congenital, but there is no convincing evidence that it is ever inherited. Not uncommonly ready bruising and other forms of bleeding can be traced through other members of the family tree, but the entire subject of inheritance is beclouded through lack of adequate laboratory data.

HEMATOLOGY

Marked thrombocytopenia is the only constant hematologic feature of the blood. The bleeding time,

6. Troland, C. E., and Lee, F. C.: Bull. Johns Hopkins Hosp. **62:** 85 (Jan.) 1938.

7. Squier, T. L., and Madison, F. W.: J. Allergy **8:** 143 (Jan.) 1937.
8. Nickerson, D. A., and Sunderland, D. A.: Am. J. Path. **13:** 463 (May) 1937.

while usually prolonged, has not infrequently been normal in our cases. The clotting time is normal but the clot usually fails to retract. The white cell count may be normal or there may be a mild or moderate increase in polymorphonuclear leukocytes, depending on the severity and recency of hemorrhage. The red cell count and degree of reticulocytosis depend directly on the amount of blood loss. The tourniquet test is usually positive; occasionally, however, it is completely negative even when platelet values are very low.

There is no abnormality in the bone marrow except that which may reflect rapid and excessive loss of blood. The megakaryocytes have never been numerically decreased or qualitatively altered in our cases of true essential thrombocytopenic purpura. Increase in these elements is common. The accompanying table presents the average of twenty-one bone marrow counts in eleven patients preoperatively and the average of fifteen bone marrow counts postoperatively in six patients.

DIFFERENTIAL DIAGNOSIS

The separation of this disease entity from the host of other abnormalities that present bleeding with thrombocytopenia is often a difficult diagnostic problem. Failure to accomplish this maneuver successfully may result in disastrous therapeutic decisions and has, in general, canceled much of the statistical value of the literature. Less attention should be paid to the tourniquet test, clot retraction and bleeding times and more to the diagnostic features given below. The examination of the cellular content of the bone marrow we regard as essential before final diagnosis is made in any given case.

Diagnostic essentials:

1. There must be spontaneous purpura and/or free bleeding from the mucous membranes.
2. The blood platelets must be substantially decreased in numbers, less than 100,000 per cubic millimeter of blood.
3. The clotting time and prothrombin time must be within normal limits.
4. The anemia and leukocyte count must not be out of proportion to the amount of bleeding.
5. There must be no pathologic cells in either the blood or the bone marrow.
6. There must be no recent history of the ingestion of drugs or the occurrence of those diseases known occasionally to produce thrombocytopenia.
7. There must be no appreciable enlargement of the spleen or lymph nodes.

COURSE

In the untreated case, the disease is often characterized by a cyclic course of remissions and exacerbations. Some patients may not have a recurrence of the disease after remission; others may be free for several years only to suffer a relapse later when they regarded themselves permanently cured. In most cases, however, a more or less chronic state ensues with varying degrees of disablement. There does not seem to be any correlation between the severity of the bleeding episode and the subsequent course. In Wintrobe's [9] series (eighteen cases) the interval between the first bleeding episode and the second varied from one month to twenty-six years.

9. Wintrobe, M. M.; Hanrahan, E. M., Jr., and Thomas, C. B.: Purpura Haemorrhagica, with Special Reference to Course and Treatment, J. A. M. A. **109:** 1170 (Oct. 19) 1937.

TREATMENT

There have been few diseases in which the status of treatment has been so confused as that of essential thrombocytopenic purpura. This uncertainty has apparently been due in part to errors in differential diagnosis and in part to the failure to appreciate the remarkable tendency of the disease to subside spontaneously.

1. *Medical.*—Radiant Energy: Chief among the forms of radiant energy employed is that of high voltage roentgen therapy over the spleen. This method of treatment, first suggested by Stephan [10] and more recently reviewed by Rudisill [11] and others, has been variously reported as successful [12] and unsuccessful.[13] Our own experience has convinced us that it is worthless (charts 2, 4 and 5). Ultraviolet rays, advocated by Sooy and Moise,[14] have been of no service in our hands nor in those of most others.[15]

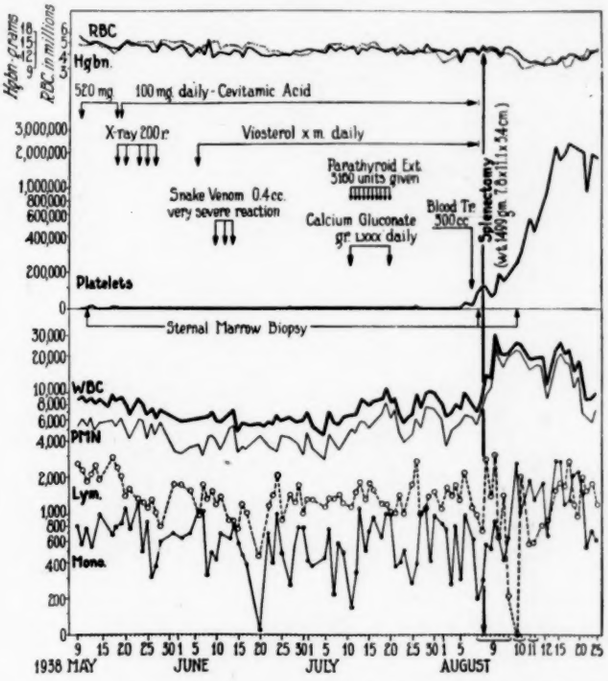

Chart 4 (Z. L., a woman aged 48).—This chart shows, on the same patient, the effects of a number of therapeutic agents variously stated to be of value in thrombocytopenic purpura, and the effects of spontaneous remission and coincident splenectomy. No increased platelet level was observed for ten days after the parathyroid extract treatment had been discontinued. Spontaneous remission then occurred with rising platelet levels. Three days later the platelet level was at 104,000 and splenectomy was accomplished at this level. Under the circumstances of the combined effect of spontaneous remission plus splenectomy, neither the speed in recovery of platelets nor the height to which they soared was greater than in the average case under the effects of splenectomy alone.

Snake Venom: The use of snake venom (Peck and Rosenthal [16]) has been suggested both as a means of controlling hemorrhage and as a prognostic test. For treatment from 0.4 cc. to 1 cc. of 1:3,000 moccasin venom is given subcutaneously twice weekly. In Rosen-

10. Stephan, R.: München. med. Wchnschr. **67:** 309 (March 12) 1920.
11. Rudisill, H., Jr.: Successful Treatment of Essential Thrombopenia with Hemorrhage by Roentgen Rays, J. A. M. A. **107:** 2119 (Dec. 26) 1936.
12. Mettier, S. R., and Stone, R. S.: Am. J. M. Sc. **191:** 794 (June) 1936.
13. Jones, H. W.; Tocantins, L. M., and Smith, R. M.: Ann. Int. Med. **11:** 1311 (April 7) 1938.
14. Sooy, J. W., and Moise, T. S.: Treatment of Idiopathic Purpura Haemorrhagica by Exposure to Mercury Quartz Lamp: Preliminary Report, J. A. M. A. **87:** 94 (July 10) 1926.
15. Tolstoi, Edward: Purpura Haemorrhagica (Essential Thrombocytopenia): Treatment by Mercury Vapor Lamp, J. A. M. A. **89:** 370 (July 30) 1927.
16. Peck, S. M.; Rosenthal, Nathan, and Erf, L. A.: Value of Prognostic Venom Reaction in Thrombocytopenic Purpura, J. A. M. A. **106:** 1783 (May 23) 1936.

thal's series of thirty-four chronic cases twenty-two were improved clinically without any improvement in the platelet levels; the remainder were refractory. The prognostic test is performed by injecting from 0.1 to 0.2 cc. of 1:3,000 moccasin venom intracutaneously. The trend from a positive test to a negative one is said to be of value in estimating the trend of the purpuric state and the prognosis after splenectomy. According to Peck and Rosenthal, patients treated with the snake venom without reversal of the positive skin test to negative are likely to obtain little benefit from surgery. Their experience needs verification from other clinics and further experience before the status of venom therapy is established. In our own hands, with a very limited experience, the use of snake venom has not been encouraging (charts 3 and 4).

Parathyroid Extract: Lowenburg and Ginsburg [17] observed a case of this disease in which the patient received an overdose of parathyroid extract consisting of 500 units in five days. During this time all bleeding stopped. A second case was reported in 1936 [18] in which 60 units of parathyroid extract plus calcium gluconate were given intentionally to a 7 year old boy with improvement clinically and hematologically. The treatment as outlined by these authors consists in giving parathyroid extract plus calcium gluconate to the point of intoxication in which symptoms of vomiting, progressive weakness, apathy and lethargy predominate. This treatment has been tried in our clinic without any favorable results (chart 4).

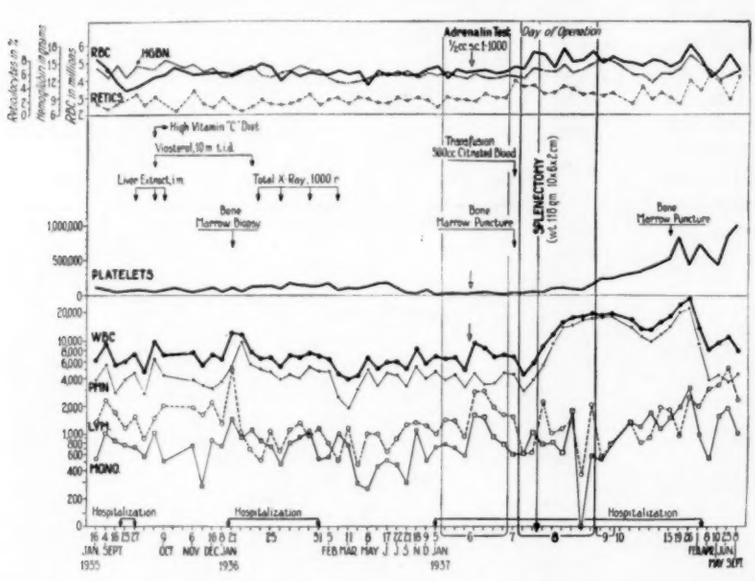

Chart 5 (M. K., a woman aged 50).—This chart illustrates the results of various therapeutic procedures in a very chronic case of thrombocytopenic purpura followed with blood counts over a period of three years, during which time the platelets at no time exceeded 200,000. Splenectomy resulted in a prompt restoration of normal numbers of platelets to the circulating blood.

Elimination Diets: This is discussed under pathogenesis. The suggestions of Madison and Squier have not been verified in our experience (chart 2).

Transfusion: The value of blood transfusions has been accorded wide acceptance, although Brill and Rosenthal [19] have indicated that an increase of hemorrhage may follow transfusion, especially in acute cases, an event which we have not observed. Blood transfusion supplies not only lost plasma volume and red cells but adds also platelets presumably useful in controlling the loss of blood. The practical value of the latter may be open to serious question, but of the former there can scarcely be any doubt. Transfusion has no effect in reestablishing the platelet equilibrium and, therefore, can in no sense be regarded as a curative measure but does serve the purpose of carrying the patient until a spontaneous remission sets in or of preparing the patient for operation so that the surgical risk will be less formidable. In some cases there is a variable hemostatic effect exerted by the transfusions which may be effective for from two to four days. Transfusions, when used, should be given in full doses (500 cc. for those of adult ages) and repeated as often as necessary to: (1) control excessive bleeding, (2) keep the blood pressure above 90 systolic and (3) maintain the red count above 2,000,000. Citrated blood given by the indirect technic is as effective as direct infusions of whole blood. Injections of blood intramuscularly are not of value.

Miscellaneous Measures: The injection of foreign proteins, calcium, proprietary coagulants, epinephrine and the like are without value in this disease. The use of viosterol by mouth has not helped in our cases. Intravenous injections or per oral use of ascorbic acid [20] recently advocated has not been of service in other cases [21] nor in our series (charts 4 and 5). The use of the vitamin substances B_2 and A [22] and endocrine extracts, particularly thyrotropic hormone,[23] needs confirmation.

2. *Surgical.*—Splenectomy: Since the demonstration by Kaznelson and Hess that splenectomy is regularly followed by a return of platelets to the blood stream and the cessation of bleeding, the constancy of this therapeutic result has been amply verified. The dramatic results of removal of the spleen with cessation of hemorrhage, often while the patient is still on the operating table, with a rise of platelets beginning immediately and more often than not reaching normal values in from twenty-four to forty-eight hours, leave one with little doubt that the measure is a specific and not a symptomatic one. The chief problem referable to splenectomy becomes a matter of individual judgment as to procedure based on the circumstances surrounding a given individual case. Here, as elsewhere, the wisdom of "treating the patient and not the disease" must not be neglected. The essence of all medical management in this disorder is clearly one of sustaining the patient until a remission occurs. If bleeding does not subside or tend to diminish in the chronic case within a week it would appear unwise to delay surgery further, as it must be accepted as a cardinal principle in the management of this disorder that the more prolonged or violent the bleeding the more danger of a sudden fatal termination through cerebral hemorrhage or bleeding into some other vital structure.

17. Lowenburg, Harry, and Ginsburg, T. M.: Acute Hypercalcemia: Report of Case, J. A. M. A. **99**: 1166 (Oct. 1) 1932.
18. Lowenburg, Harry, and Ginsburg, T. M.: Induced Hypercalcemia: Its Possible Therapeutic Relation to Thrombocytopenic Purpura, J. A. M. A. **106**: 1779 (May 23) 1936.
19. Brill, N. E., and Rosenthal, Nathan: Treatment by Splenectomy of Essential Thrombocytopenia, Arch. Int. Med. **32**: 939 (Dec.) 1923.
20. Miller, D. K., and Rhoads, C. P.: J. Clin. Investigation **15**: 462 (July) 1936.
21. Stephans, J. J., and Hawley, Estelle E.: J. Lab. & Clin. Med. **22**: 173 (Nov.) 1936.
22. von Schiff, E., and Hirschberger, C.: Jahrb. f. Kinderh. **146**: 191 (Feb.) 1936.
23. Zondek, Hermann, and Kaatz, A.: Brit. M. J. **2**: 387 (Aug. 22) 1936.

The acute cases especially demand energetic action. Most authors warn against splenectomy in the acute phases of this disease. Our experience, however, has been quite favorable. In our opinion, the incipient acute type as well as the acute exacerbation of the chronic type is an especial indication for urgent surgery, as a goodly proportion of this group will die otherwise. The procedure followed in our clinic may be summarized as follows:

1. The diagnosis must be confirmed in all cases by bone marrow examination (puncture technic).

2. Blood transfusions are always given immediately if active bleeding presents.

(*a*) If this is effective in stopping hemorrhage after a reasonable trial, delay in advising splenectomy is justified. If the platelet level, determined daily, rises and continues to rise, plans for splenectomy may be temporarily or permanently abandoned, depending on subsequent improvement.

(*b*) If blood loss persists in acute cases in the same or in increased volume, splenectomy is not postponed further.

3. Splenectomy is indicated in:

(*a*) Chronic cases if free bleeding persists after a reasonable period of treatment with transfusions or when social or economic factors are important.

(*b*) Acute cases when transfusion is not immediately effective.

4. Splenectomy is contraindicated in:

(*a*) Cases of doubtful diagnosis.

(*b*) Cases presenting a recent history of contact with certain drugs.

(*c*) Cases occurring during the active or convalescent stages of all infectious diseases.

(*d*) Cases in which the bone marrow shows depletion of the megakaryocytic content of the bone marrow.

Splenic Artery Ligation: This procedure probably should never be attempted in purpura haemorrhagica. Although the procedure may stop the bleeding,[24] this is not to be relied on. The spleens in this disease are small and free from adhesions and are removed with very little more technical difficulty and risk to the patient than the procedure of ligation of the artery.

PROGNOSIS

It is clear that the results in the surgical group of cases vary markedly from clinic to clinic. In our clinic during the past five years there have been nine cases in which splenectomy has been done. One of the patients died of postoperative shock. The others are well at the present time. This is a small series and obviously cannot be used statistically. Surgical deaths will inevitably occur but should not exceed 5 per cent (Giffin's experience[25]). The liberal use of blood transfusions preoperatively, and postoperatively if required, the adequacy of differential diagnosis and good technical surgery should make it possible to duplicate this low operative mortality in most hospitals.

If not operated on, of those patients in whom bleeding is severe enough to warrant surgery, probably 30 per cent will die (Giffin series 27 per cent). Of those operated on, not more than 3 per cent will have recurrences.

It is not possible to say what the surgical mortality would be in those chronic cases in which expectant or medical treatment is given as they are not usually submitted to surgery. It is obvious that the cases submitted to surgery usually represent the most dangerous risks, which fact tends to weight the surgical mortality to the advantage of the medically treated group. Wintrobe's figures in a series of forty-seven cases at the Johns Hopkins Clinic[9] in which medical treatment was started after the patient had had the first episode of bleeding showed as late results that 70 per cent continued to have symptoms and signs of varying degree.

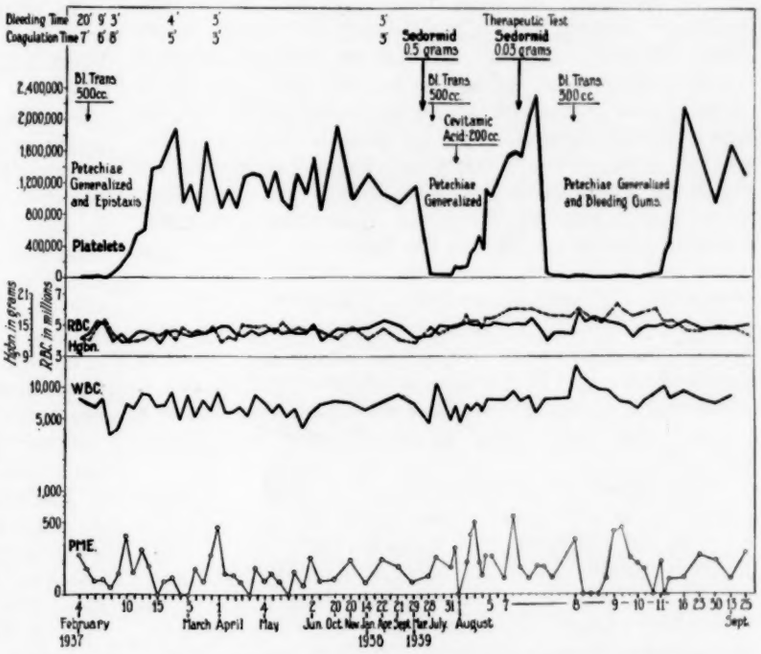

Chart 6 (E. F., a woman aged 57).—This is a case of secondary (symptomatic) thrombocytopenic purpura illustrating the specific platelet-reducing effects of allyl-isopropyl-acetyl-carbamide (sedormid). The patient was admitted to the hospital first in 1937 with the history of ingestion of "barbiturates" and recovery ensued as shown. In July 1939 the patient was again hospitalized with severe thrombocytopenia and hemorrhagic manifestations after having taken 0.5 Gm. of allyl-isopropyl-acetyl-carbamide. After recovery 0.03 Gm. of the drug was given as a test dose. Following a preliminary rise in platelets from 1,600,000 to 2,400,000 per cubic millimeter of blood, these elements fell precipitously to practically zero levels in six hours. Four days elapsed before the platelets reappeared in appreciable numbers. Within twenty-four hours, however, the platelet level was over 800,000 per cubic millimeter of blood.

SUMMARY

1. No single theory for the production of essential thrombocytopenic purpura adequately accounts for all the known facts relating to this disease; however, that of splenic thrombocytolysis appears to violate the fewest.

2. In differential diagnosis, aspiration of bone marrow to rule out leukopenic leukemia, aplastic anemia, pernicious anemia and neoplasia is at times essential. Historical facts relating to drugs and present or recent contact with certain infectious diseases are most important.

3. In essential thrombocytopenia, the only measure known that will restore the platelet level is splenectomy. The more pronounced the bleeding tendency the more urgent the indication for surgery.

4. No case of symptomatic thrombocytopenia, regardless of the degree of bleeding, should be submitted to surgery.

Kinsman Hall.

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TREATMENT OF HYPOPROTHROMBINEMIA HAEMORRHAGICA NEONATORUM

(HEMORRHAGIC DISEASE OF THE NEWBORN) WITH VITAMIN K

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More than 250 years has elapsed since the first case of hemorrhagic disease of the newborn was recorded in medical literature and a specific form of treatment was discovered. The events leading up to this discovery form a fascinating chapter in the history of medicine and have recently been reviewed in detail elsewhere.[1] While excellent contributions on the nature of the disease had been made by Lespinasse and Fischer,[2] Schloss and Commiskey,[3] Whipple,[4] Løvegren,[5] Rodda,[6] Gelston[7] and others, the fundamental observation that served as the impetus for the solution of the exact pathogenesis and treatment of the disease was the investigative work of Henrik Dam, of Denmark.[8] Dam, in the course of biochemical investigations on sterol metabolism in chicks, found that when they were fed a fat-free diet fatal hemorrhage resulted. Further study showed that the hemorrhagic manifestations were associated with low levels of plasma prothrombin. Because the unknown substance, which was apparently lacking in a fat-free diet, interfered with normal coagulation of the blood, Dam suggested the name vitamin K (K for the Danish word koagulation). Phenomenal progress in the purification and isolation of the antihemorrhagic factor, vitamin K, quickly followed.

Final steps in the application of vitamin K as a prophylactic and curative measure in hemorrhagic disease of the newborn were initiated with the development of satisfactory methods for the quantitative determination of the blood prothrombin level.[9] Then followed the reemphasis and conclusive demonstration of low prothrombin values in the blood of normal infants as compared with adults[10] and the extreme lowering of prothrombin levels in infants with hemorrhagic disease of the newborn. Later, a transitory hypoprothrombinemia in normal infants was demonstrated between the second and the sixth day of life.[11] This finding explained the earlier observation of Rodda,[6] who reported prolongation of the clotting time during the same period of life. Finally it was shown that this transitory hypoprothrombinemia and the absolute prothrombin deficiency in infants with hemorrhagic disease of the newborn could be corrected by the administration of vitamin K.

Thus a new era in the treatment of hemorrhagic disease of the newborn may be said to have begun with the work of Waddell, Guerry, Bray and Kelley,[12] who successfully demonstrated the therapeutic effect of vitamin K in two cases of this disease. Their observation was followed by a communication by Waddell and Guerry[13] on the influence of vitamin K concentrate in shortening the prothrombin clotting time of ten newborn infants as compared with the prothrombin time in untreated babies. These authors[14] further reported eight additional cases of hemorrhagic disease of the newborn, all of which, with the exception of one fatal case, responded to vitamin K therapy with uneventful recovery. A confirmation of these experiences has recently been published by Nygaard[15] and by Dam and his co-workers.[16] From these reports, few as they are, it now appears reasonable to conclude that a fundamental defect in the prothrombin activation of the blood is directly responsible for the bleeding tendencies characteristic of the symptomatology of hemorrhagic disease of the newborn. On etiologic grounds Nygaard proposed the term "hypothrombinemia haemorrhagica neonatorum," but more accurately the disease should be designated as "hypoprothrombinemia haemorrhagica neonatorum," since the defect lies in the prothrombin activation of the blood.

The evidences proving the specific effect of vitamin K in controlling the concentration of blood prothrombin in such conditions as obstructive jaundice, diseases of the liver and certain deficiency diseases of chicks and cattle are rapidly multiplying in the literature. Reports on the therapeutic efficacy of this vitamin on hemorrhagic disease of the newborn, however, are still limited in number, so that additional experiences in this particular field must be obtained in order to make its general use more intelligently recommendable both in obstetric and in pediatric practice. The present communication is intended merely to contribute additional data on the treatment of hypoprothrombinemia of the newborn with vitamin K and its substitutes.

A total of twenty-two cases of hemorrhagic disease of the newborn forms the basis of the present report. In all these cases the prothrombin clotting time was

This study was aided by a grant from Mead Johnson & Co.

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Drs. A. H. Parmelee and Joseph Greengard of the Cook County Children's Hospital, Dr. F. H. Falls, head of the Department of Obstetrics and Gynecology, Research and Educational Hospitals, and Dr. Fred A. Adair, chairman of the Department of Obstetrics and Gynecology, Chicago Lying-in Hospital, gave the authors permission to use patients in their respective departments for this study.

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determined by the micromethod of Kato [17] both before and after the institution of vitamin K therapy. In many instances several follow-up determinations were made at daily intervals for a period of three or four days. The results of these observations are summarized in the accompanying tables.

All the cases included in this series exhibited typical clinical symptoms of bleeding, conforming to the usual description of the disease as reviewed recently

TABLE 1.—*Symptoms of Hypoprothrombinemia Haemorrhagica Neonatorum in Twenty-Two Cases*

Case	Age at Onset, Hours	Symptoms	Prothrombin Time: Before Treatment, Seconds	Prothrombin Time: 24 Hours After Treatment, Seconds	Vitamin K, Form, Dose, Route *
1	50	Hematemesis	160	27	K_3, (F. S.), 10 mg., oral
2	68	Hematemesis, omphalorrhagia	272	32	K_3, (F. S.), 10 mg., oral
3	62	Hematemesis, omphalorrhagia	300+	28	K_3, (F. S.), 10 mg., oral
4	43	Hematemesis	154	25	K_3, (F. S.), 10 mg., oral
5	49	Omphalorrhagia, melena	300+	26	K_5, 1 mg., I.M.
6	69	Omphalorrhagia, melena, hematuria, hematemesis	300+	25	K_5, 1 mg., I.M.
7	52	Omphalorrhagia	300+	27	K_5, 1 mg., I.M.
8	58	Hematemesis, dermal hemorrhage, cerebral symptoms	300+	28	K_5, 1 mg., I.M.
9	42	Hematemesis, melena	300+	24	K_5, 1 mg., I.M.
10	96	Cerebral symptoms	300+	26	K_5, 1 mg., I.M.
11	53	Hematemesis, melena	250	27	K_5, 1 mg., I.M.
12	76	Hematemesis, melena	220	26	K_5, 1 mg., I.M.
13	68	Hematemesis	246	23	K_5, 1 mg., I.M.
14	24	Hematemesis	300+	28	K_5, 1 mg., I.M.
15	38	Hematemesis, cerebral symptoms	300+	26	K_5, 1 mg., I.M.
16	40	Melena	200	22	K_5, 1 mg., I.M.
17	32	Omphalorrhagia, cephalhematoma, hematuria	300+	26	K_5, 1 mg., I.M.
18	51	Hematemesis	272	24	K_5, 1 mg., I.M.
19	42	Hematemesis, omphalorrhagia	220	25	K_3, (W. S.), 2 mg., subcut.
20	72	Hematemesis	110	34	K_3, (W. S.), 2 mg., subcut.
21	96	Dermal hemorrhage, melena, omphalorrhagia	300+	24	K_3, (W. S.), 2 mg., subcut.
22	72	Hematemesis	300+	20	K_3, (W. S.), 2 mg., subcut.

* F. S. = fat slouble; W. S. = water soluble; I.M. = intramuscularly; subcut. = subcutaneously.

by Javert,[18] Clifford,[19] Salomonsen [20] and Quick and Grossman.[21]

The frequency of clinical forms of bleeding in the present series was as follows: hematemesis sixteen cases, melena eight cases, omphalorrhagia eight cases, dermal or cutaneous hemorrhage three cases, cerebral symptoms three cases and hematuria two cases. In the majority of instances two or three of these symptoms occurred in the same case.

The average time of onset of hemorrhagic manifestations was fifty-four hours after birth, the earliest being twenty-four hours and the latest ninety-six hours. The distribution of the disease as to race and sex was as follows: white thirteen patients, Negro nine patients; male fifteen patients and female seven patients.

The average prothrombin clotting time in ten cases before treatment was 210 seconds, the shortest being 110 seconds and the longest 272 seconds. In twelve cases before the institution of vitamin therapy the prothrombin time was prolonged beyond five minutes.

The average prothrombin time for all cases during the twenty-four hours following treatment was reduced to twenty-six seconds. In most of the cases, shortening of the prothrombin time could be demonstrated within from two to six hours after the administration of the antihemorrhagic vitamin.

TABLE 2.—*Prothrombin Time Before and After Treatment*

Case	Before Treatment, Seconds	After Treatment with Vitamin K: 2 Hrs., Seconds	6 Hrs., Seconds	24 Hrs., Seconds	48 Hrs., Seconds	72 Hrs., Seconds	96 Hrs., Seconds
1a	160	80	36	27	26	24	24
2a	272	124	39	32	28	26	27
3a	300+	300+	65	28	27	25	24
4a	154	130	50	25	24	24	22
5b	300+	212	90	26	25	26	24
6b	300+	...	..	25	..	..	..
7b	300+	140	65	27	26	23	25
8b	300+	...	..	28	..	..	..
9b	300+	186	42	24	24	23	24
10b	300+	170	36	26	..	..	..
11b	250	148	40	27	26	25	24
12b	220	78	34	26	25	24	23
13b	246	...	..	29	..	..	..
14b	300+	217	36	28	26	25	26
15b	300+	210	43	26	24	25	23
16b	200	124	33	22	23	22	22
17b	300+	120	..	26	..	..	..
18b	272	63	30	24	..	..	..
19c	220	90	34	25	25	24	24
20c	110	..	..	34	30	..	..
21c	300+	..	..	24	..	..	..
22c	300+	..	..	20	..	..	..

a = K_3, (F. S.), oral, 10 mg.; b = K_5, intramuscular, 1 mg.; c = K_3, (W. S.), subcutaneous, 2 mg.

The preparations of vitamin K [21a] used in our series were (1) 2 methyl-1, 4 naphthoquinone (vitamin K_3), (2) 2 methyl-4 amino naphthol hydrochloride (vitamin K_5) and (3) solution of 2 methyl-1, 4 naphthoquinone in sodium bisulfite. The fat soluble preparation (1) was administered by mouth and the water soluble preparations (2) and (3) were given intramuscularly and subcutaneously. While water soluble preparations can be effectively given intravenously, the most accessible routes of administration were purposely chosen for practical reasons.

Neither intravenous nor intramuscular blood was used, since in none of the cases did any sign of severe posthemorrhagic anemia develop. Subcutaneous injections of fluid were given only in the limited number of cases in which pronounced dehydration was exhibited.

In all cases the clinical improvement was both prompt and permanent, and the therapeutic effects of the several vitamin preparations used were practically identical.

COMMENT

Certain features of hypoprothrombinemia haemorrhagica neonatorum as treated by vitamin K deserve special comment. The most important of these, both

17. Kato, Katsuji: Microprothrombin Test with Capillary Whole Blood: A Modification of Quick's Quantitative Method, Am. J. Clin. Path. **10:** 147 (Feb.) 1940.

18. Javert, C. T.: Hemorrhagic Disease of the Newborn, Am. J. Obst. & Gynec. **35:** 200 (Feb.) 1938.

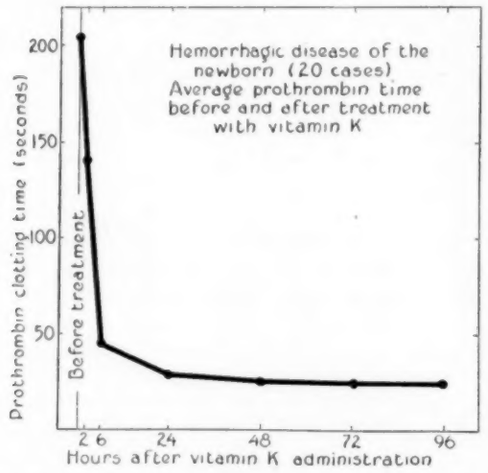
19. Clifford, S. H.: Hemorrhagic Disease of the Newborn: A Critical Consideration, J. Pediat. **14:** 333 (March) 1939.

20. Salomonsen, Leif: Morbus Hemorrhagicus Neonatorum (Hypoprothrombinemia Neonatorum), Acta pædiat. (supp. I) **27:** 5, 1939.

21. Quick, A. J., and Grossman, A. M.: The Nature of the Hemorrhagic Disease of the Newborn, Am. J. M. Sc. **199:** 1 (Jan.) 1940.

21a. Preparations 1, 2 and 3 were supplied by Mead Johnson & Co., Parke, Davis & Co. and Abbott Laboratories, respectively.

for diagnosis and for prognosis, are the changes that take place in the prothrombin clotting time of the blood. In a recent study of 173 newborn infants [22] it was found that the average prothrombin time on the first day of life, as determined by the micromethod, was 43.2 seconds for the normal mature infants and 46.5 seconds for the premature infants.[23] These values decreased with the growth of the infants, so that by the sixth to the tenth day of life the majority of the infants showed the average normal prothrombin time of approximately twenty-five seconds. In both clinical and subclinical cases of hypoprothrombinemia in the newborn the prothrombin clotting time was markedly prolonged, the average time in ten of our twenty-two cases being 210 seconds. In twelve cases of our series no end point in the microprothrombin tests performed before treatment was recognizable. In other words, when the prothrombin clotting time is prolonged beyond two minutes by the micromethod, even in the absence of clinical symptoms, a presumptive diagnosis of subclinical hypoprothrombinemia must be made. Such an abnormal prolongation of prothrombin time signifies a state of vitamin K deficiency, and replacement therapy is indicated.



Average prothrombin time of twenty of the twenty-two infants before and after treatment with vitamin K.

The specificity of synthetic preparations with vitamin K activity in the restoration of prothrombin activation to its normal level is conclusively proved by our observations, since all cases without exceptions and regardless of the preparations used and the routes of administration responded to the therapeutic action of this vitamin. The efficacy of the treatment with vitamin K appears to be both prompt and permanent. After a single administration of the vitamin, in doses varying from 1 to 10 mg., the prothrombin times dropped within six hours to almost normal levels, as shown in the accompanying chart. The vitamin K preparations used in our series were limited in number, but it is reasonable to expect any chemical substitute embodying vitamin K activity to produce similar effects on the prothrombin time of the blood. The water soluble analogues of vitamin K used in this study can be injected intravenously with absolute safety, although such a procedure is usually not necessary, since intramuscular or even subcutaneous administration is promptly effective. Various pharmaceutic concerns, now busily engaged in their preparations and assays, expect to offer to the profession a number of water soluble esters of vitamin K. Once the effect of the vitamin has taken place, as evidenced by both cessation of hemorrhage and shortening of the prothrombin time, there is practically no tendency for the clinical signs to reappear. Furthermore, unless the case is complicated by severe posthemorrhagic anemia, the promptness and permanence in the correction of hypoprothrombinemia with vitamin K make blood transfusions unnecessary. In the event of a serious loss of weight or evidence of pronounced dehydration, subcutaneous injections of fluid may be indicated.

Finally it must be emphasized that, in order to treat hypoprothrombinemia in the newborn effectively, an early and correct diagnosis is imperative. In this connection a grouping of hypoprothrombinemia in the newborn into clinical and subclinical types is suggested. The infants who show both the prolongation of blood prothrombin time and actual manifestations of hemorrhage belong to the clinical type of hypoprothrombinemia, while those with only the prolongation of prothrombin time and no clinically demonstrable signs of bleeding constitute the subclinical group. It is indisputable that both forms of hypoprothrombinemia are due to vitamin K deficiency, differing only in degree of such deficiency; hence the specific therapy required is identical in the two groups.

The microprothrombin test recently described by Kato and employed throughout our investigation has been found to be entirely satisfactory and admirably suited for the diagnosis of hypoprothrombinemia in the newborn, since only a small amount of capillary blood is required for the tests, thus facilitating its repetition at frequent intervals on the same patient. The coagulation and bleeding times which customarily serve as diagnostic tests in hemorrhagic diatheses may be prolonged in conditions other than hypoprothrombinemia. It is therefore essential in order to establish the diagnosis of hypoprothrombinemia, whether clinical or subclinical in type, to determine the blood prothrombin time. Moreover, it is safe to expect that frequent or even routine determinations of prothrombin clotting time will result in more frequent detection of subclinical hypoprothrombinemia in the newborn, a condition which may be regarded as a potential or latent form of hemorrhagic disease. It is only with the adoption of such a routine that one can definitely control hemorrhagic tendencies in the neonatal period and thereby reduce the incidence of infant deaths.

SUMMARY AND CONCLUSIONS

Twenty-two infants with hypoprothrombinemia haemorrhagica neonatorum (hemorrhagic disease of the newborn) were successfully treated with synthetic preparations of vitamin K. The infants exhibited the typical clinical manifestations of hematemesis, melena, omphalorrhagia, dermal hemorrhage, hematuria and cerebral symptoms prior to treatment.

In all cases the determinations of prothrombin clotting time by the micromethod were made both before and after the institution of treatment. The average

22. Kato, Katsuji, and Poncher, H. G.: The Prothrombin in the Blood of Newborn Mature and Immature Infants as Determined by the Microprothrombin Test, J. A. M. A. **114**: 749 (March 2) 1940.

23. These figures represent average determinations done on infants from birth to 24 hours. It was impossible to get the values at birth or immediately thereafter consistently because neither of the authors was resident in the hospital. Consequently, the usual lowering of prothrombin time noted in many infants during the first twelve hours after birth, as reported by other investigators, was obscured.

prothrombin time of ten patients giving a definite end point before treatment was 210 seconds, while in twelve cases the time was prolonged beyond five minutes.

Three synthetic preparations of vitamin K were employed: (1) 2 methyl-1,4 naphthoquinone (vitamin K_3), (2) 2 methyl-4 amino naphthol hydrochloride (vitamin K_5) and aqueous solution of 2 methyl-1,4 naphthoquinone with sodium bisulfite. These drugs were administered orally, intramuscularly and subcutaneously, in the order named, immediately on a definite diagnosis of hemorrhagic disease of the newborn being confirmed by a prolonged prothrombin time. In most of these cases the effect of therapy was demonstrated by the shortening of the prothrombin time within two to six hours after medication. Clinical improvement was both prompt and permanent with all preparations tested.

In none of the cases were blood transfusions given, prompt cessation of bleeding following therapy having caused no alarming loss of blood with consequent anemia. Subcutaneous injections of fluid were employed only in the presence of loss of weight or pronounced dehydration.

From these observations it may be concluded that vitamin K and its esters are specific in the treatment of hypoprothrombinemia haemorrhagica neonatorum.

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LYMPHOSARCOMA

A STUDY OF 196 CASES WITH BIOPSY

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Lymphosarcoma is a malignant neoplastic disease of lymphoid tissue capable of arising in any lymphoid aggregate. It may run an acute or chronic course and is almost invariably very radiosensitive. An apparent cure is possible but the disease is much more likely to terminate in death, at which time the wide extent of clinically unsuspected metastases may be astonishing.

With Hodgkin's disease and lymphatic leukemia, it comprises a group of tumors of relatively low morbidity, the high mortality and often strikingly similar clinical and pathologic pictures of which have properly earned them the designation "malignant lymphomas." The term "lymphoblastoma" (Desjardins,[1] Minot and Isaacs[2]) has gained considerable popularity as a means of rather loosely conjoining a number of conditions of which lymphosarcoma and Hodgkin's disease make up the majority. The practicality and convenience of any term aimed at accomplishing such a linkage cannot be denied when applied to individual cases in which identical clinical settings and often very similar histologic pictures make clearcut differentiation almost impossible, and only as a reminder of these occasional difficulties does the term deserve any merit at all. By implying a common genesis of the two diseases for which there is actually no justified foundation it has brought about in reported papers a merging of the two conditions in which the distinctive features of each have been lost.

It is our purpose in this paper not to reestablish the separate identities of lymphosarcoma and Hodgkin's disease by any form of detailed differential comparison but rather to present a study of the first named condition by itself, based on a series of 196 cases of lymphosarcoma in each of which the diagnosis was confirmed by biopsy. Moreover, in order to insure uniformity of material no case was included in the group unless diagnosis of the pathologic section had been confirmed at this hospital.

HISTORY

The first recognition of lymphosarcoma as a disease entity to be distinguished from the aleukemic lymphomas (pseudoleukemia) is credited to Kundrat[3] (1893). In the succeeding decades various writers attempted to subdivide the aleukemic lymphomas into different distinct types, but the seemingly insurmountable difficulties of drawing sharp lines of demarcation between types and the apparent transition from one type to another have probably led to greater confusion in this branch of oncology than in any other. The concept of lymphosarcoma has not escaped this confusion. From the former simple classification of large and small cell lymphosarcoma, some progress was made in distinguishing between recticulum cell lymphosarcoma[3a] and malignant lymphocytoma. The giant follicular lymphadenopathy described by Brill, Baehr and Rosenthal[4] and by Symmers[5] is usually regarded as bearing some relation to lymphosarcoma, though as yet this relation is not clearly defined, nor has the scope of "Brill-Symmers disease" been adequately determined. The borderlines between lymphosarcoma and lymphatic leukemia, Hodgkin's disease, mycosis fungoides and the reticuloses remain rather shadowy at present. As a reaction to this confusion, the lumping together of thirteen or more different terms into a general category of lymphoblastoma seems an unfortunate defeatist step, hardly serving to make progress in understanding the natural history of what are probably different processes.

MORBID ANATOMY

Just as other tissues may assume malignant properties, so lymphoid tissue is capable of attaining this pathologic mode of expression. The sites of origin of lymphosarcoma are potentially as widespread as is the distribution of lymphoid aggregates throughout the body. The unit of lymphoid tissue, the lymph follicle, being composed of two distinct and easily identified types of cells (the reticulum or endothelioid cells of the germinal center, and the small lymphocytes arranged peripherally about these centers), may give rise to two corresponding histologic types of sarcoma: the reticulum cell type, or reticulum cell lymphosarcoma, illustrated in figure 1, and the lymphocytic type, or malignant lymphocytoma, shown in figure 2 (Ewing[6]). The

From the Memorial Hospital for the Treatment of Cancer and Allied Diseases.

1. Decker, F. H.; Leddy, E. T., and Desjardins, A. U.: Leukopenia and Leukocytoses in Lymphoblastoma, Am. J. Roentgenol. **39:** 747 (May) 1938. Desjardins, A. U.: Radiotherapy for Hodgkin's Disease and Lymphosarcoma, J. A. M. A. **99:** 1231 (Oct. 8) 1932. Desjardins, A. U., and Ford, Frances A.: Hodgkin's Disease and Lymphosarcoma, ibid. **81:** 925 (Sept. 15) 1923. Desjardins, A. U., and Watkins, C. H.: Abdominal Lymphoblastoma and Its Treatment by Irradiation, South. M. J. **29:** 344 (April) 1936.

2. Minot, G. R., and Isaacs, Raphael: Lymphoblastoma and Malignant Lymphoma, J. A. M. A. **86:** 1185-1189 (April 17), 1265-1270 (April 24) 1926.

3. Kundrat, Hans: Ueber Lymphosarkomatosis, Wien. klin. Wchnschr. **6:** 211, 1893.

3a. Roulet, F.: Weitere Beiträge zur Kenntnis des Retothelsarkoms der Lymphknoten und anderer Lymphoiden-Organe, Virchows Arch. f path. Anat. **286:** 702, 1932.

4. Brill, N. E.; Baehr, George, and Rosenthal, Nathan: Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen, J. A. M. A. **84:** 668 (Feb. 28) 1925.

5. Symmers, Douglas: Certain Clinical and Pathologic Aspects of Lymphosarcoma, Am. J. M. Sc. **174:** 9 (July) 1927; Follicular Lymphadenopathy with Splenomegaly, Arch. Path. **3:** 816 (May) 1927; Giant Follicular Lymphadenopathy With or Without Splenomegaly, ibid. **26:** 603 (Sept.) 1938.

6. Ewing, James: General Pathology of Lymphosarcoma, Bull. New York Acad. Med., February 1939, p. 92; Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 382.

exact physiologic tie between these two cell types has not been definitely established, although their anatomic juxtaposition bolstered by the clinical observation of the not infrequent termination of reticulum cell lymphosarcoma in lymphatic leukemia strongly suggests the

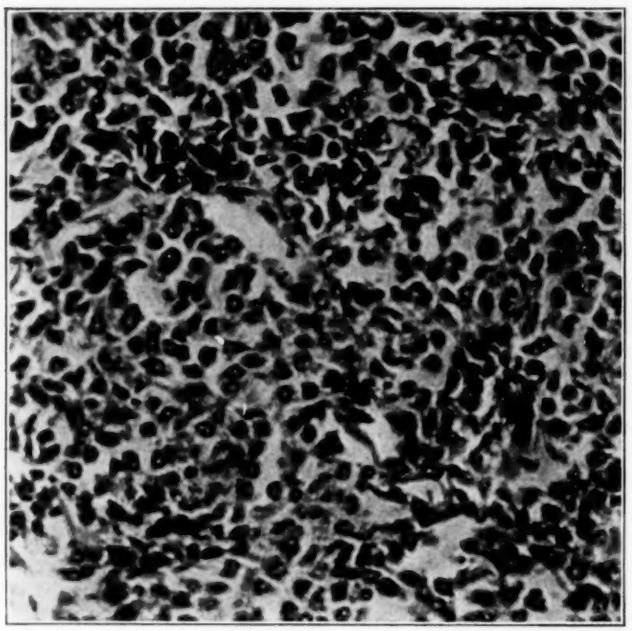

Fig. 1.—Reticulum cell lymphosarcoma (× 400), so-called large cell type; compare size of cells with size of those in figure 2.

existence of a very definite though as yet obscure relationship. It would seem reasonable therefore, until such time as proof to the contrary is found, to consider tumors composed of either cell type, exhibiting malignant properties, simply as variations of the same disease, namely lymphosarcoma.

A predominance either of the cells of the germinal center or of its surrounding lymphocytic zone early in the disease with subsequent obliteration of follicular architecture later results in complete disruption of the structure of the entire lymphoid aggregate. In the case of subepithelial follicle groups there is invasion of the underlying tissues and outward growth of tumor, which may or may not ulcerate. In the lymph nodes there is eventual penetration of the node capsule and invasion of surrounding structures. Though nuclear hyperchromatism may be observed and occasional multinucleated cells are present, it is the general rather than the cytologic picture which provides the essential characteristic. Fibrosis and the presence of a granulomatous element make the diagnosis of lymphosarcoma hazardous.

In 1925 Brill, Baehr and Rosenthal [4] and in 1927 Symmers [5] reported several cases of lymphadenopathy often accompanied by splenomegaly, in which the node picture showed "numerical and dimensional follicular hyperplasia" (Symmers). The dimensional increase in the follicle apparently results from proliferation of cells within the germinal center, which enlarges to enormous proportions, often occupying an entire low power microscopic field. This is surrounded by a thinning zone of small lymphocytes, which in many instances has been completely broken through, resulting in a fusion of germinal centers (fig. 3). Whether or not such cases represent a separate clinicopathologic entity is doubtful. Recently Symmers has stated that in certain instances, at least, a transition to Hodgkin's sarcoma or to a polymorphous cell sarcoma (lymphosarcoma) as evidenced by late biopsies, or to lymphatic leukemia as shown by successive blood counts, may eventually occur in giant follicular lymphoma. The diagnosis of Hodgkin's sarcoma made on tissue removed late in the course of a disease which earlier in its development presented a picture decidedly unlike Hodgkin's granuloma is open to serious question, more so when such tissue also fails to reveal any reactive changes reflecting the earlier influence of the supposed preexistent but now extinct granulomatous process. Such a diagnosis must therefore be based solely on the presence of giant reticulum cells. These, however, occasionally occur in certain forms of lymphosarcoma (giant reticulum cell lymphosarcoma, fig. 4). The late occurrence of a leukemic blood picture is answerable in the same manner, for this is not uncommonly observed in lymphosarcoma. Indeed, the inclination at the Memorial Hospital is to consider giant follicular lymphoma as an early setting for lymphosarcoma, usually destined to run a somewhat less acute but otherwise typical course. Late biopsies in several of our cases have all shown typical reticulum cell lymphosarcoma.

Exactly where to place Hodgkin's sarcoma (fig. 5) is difficult to decide. Callender [7] would combine it and reticulum cell lymphosarcoma into a single group called "reticulum cell sarcoma." Hodgkin's sarcoma is undoubtedly a form of reticulum sarcoma developing either late in the course of the more chronic type of Hodgkin's granuloma or earlier in the course of the more acute forms of that disease and representing a truly neoplastic response of the endothelioid cells pre-

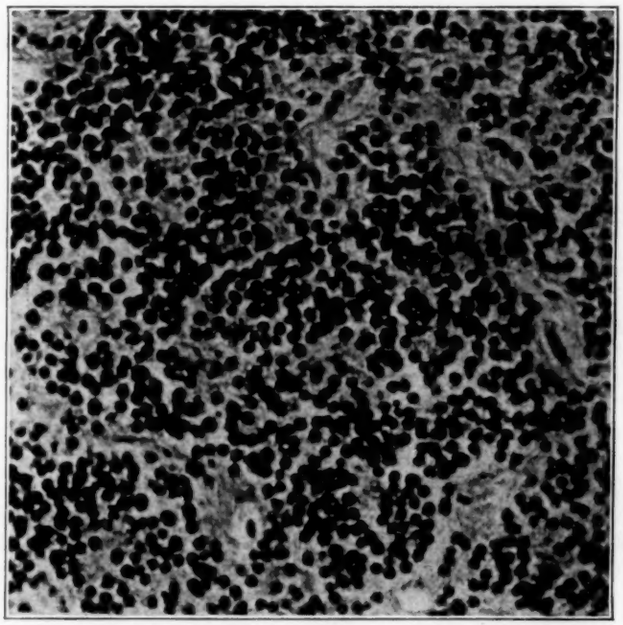

Fig. 2.—Malignant lymphocytoma (× 400), showing diffuse overgrowth of small round cells.

sumably to the exciting agent originally responsible for the chronic inflammatory reaction of the granuloma. These nodes therefore show some reactive fibrosis and perhaps a remnant of the granulomatous element in addition to the reticulum cell overgrowth. Along with

7. Callender, G. R.: Tumors and Tumor-like Conditions of the Lymphocyte, the Myelocyte, the Erythrocyte and the Reticulum Cell, Am. J. Path. **10:** 443 (July) 1934.

these distinct pathologic differences there are certain clinical variations peculiar to each which still further encourage one to allow them separate identity. For example, reticulum cell lymphosarcoma certainly appears to be a primarily malignant disease whatever its etiology,

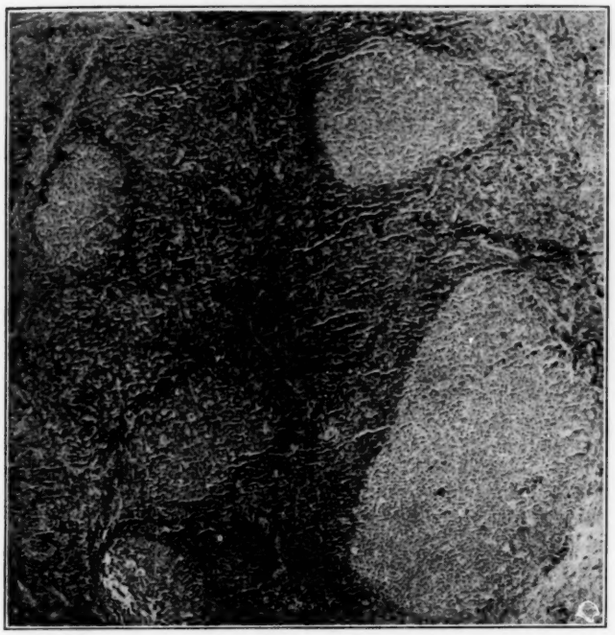

Fig. 3.—Giant follicular lymphoma, or Brill-Symmers disease (× 50), demonstrating the marked overgrowth of the follicular germinal centers with thinning and occasional disruption of the surrounding lymphocytic zone.

whereas Hodgkin's sarcoma is presumably superimposed on a granulomatous setting which may completely mask the initiation and progress of the sarcoma. More important, however, is the relationship of the former to the lymphocyte as evidenced by its not infrequent termination in lymphatic leukemia, whereas a leukemic terminus in the latter is not only much less common but is almost invariably of the monocytic type. Therefore Hodgkin's sarcoma has not been included among the cases to be presented here.

ETIOLOGY

Any clearcut statement of the biologic forces inciting lymphoid tissue to malignant growth is as impossible at present as it is for any other type of tissue. As long as histologic appearance and clinical behavior remain the most dependable criteria, it must be assumed that lymphosarcoma is a true neoplasm. Its appearance following the administration of indole [7a] and estrogens [7b] and the injection of 1,2,5,6 dibenzanthracene [7c] indicate that the mechanisms stimulating lymphoid tissue to pathologic new growth are similar to, if not identical with, those activating other tissues.

The frequency with which chronic infections are noted, particularly long-standing inflammatory processes in the upper respiratory system of patients whose first evidence of lymphosarcoma appears as a nodal swelling in the neck, is rather striking. Actually 32 per cent, whose first symptom of lymphosarcoma was cervical adenopathy, complained of some definite chronic infection of the upper respiratory tract. The role of tuberculosis, however, is much less evident in lymphosarcoma than it is in Hodgkin's disease. It is not inconceivable that prolonged stimulation of lymph nodes may eventuate in malignant cellular activity.

An equally difficult and important question concerns the monocentric versus the multicentric origin of the disease. Lymphosarcoma usually behaves differently from the ordinary forms of carcinoma in several respects. Some of this difference is undoubtedly due to the fact that the former develops within the lymphatic system, this giving it a running start on carcinoma, which must arrive there by process of secondary invasion. Involvement of a chain of lymph nodes by carcinoma is usually progressive, whereas in lymphosarcoma it is often explosive, all the nodes of the entire chain seeming to be simultaneously involved, or the disease may at once involve widely separated node groups, all of which favors the hypothesis that some very readily diffusible activating agent is responsible. On the other hand the observation that early spread of the disease most frequently occurs by means of involvement of contiguous node groups, that tumor nodules are frequently found in organs not ordinarily containing lymphoid aggregates, and that after surgical extirpation of involved nodes patients may remain permanently cured, all strongly suggest that cell emboli alone are responsible. Ewing believes that extension probably involves both dissemination of an exciting agent and cell embolism.

INCIDENCE

Lymphosarcoma occurs less frequently in this clinic than Hodgkin's disease in the ratio of 3 : 4. Males are more frequently affected than females in the ratio of about 7 : 3 (1.4 : 1 in Hodgkin's disease [7d]). The average age of the two sexes at the time of admission to the hospital was approximately the same, 45 and 45.3 years respectively, about ten years higher than in Hodgkin's disease and somewhat lower than that for the commoner

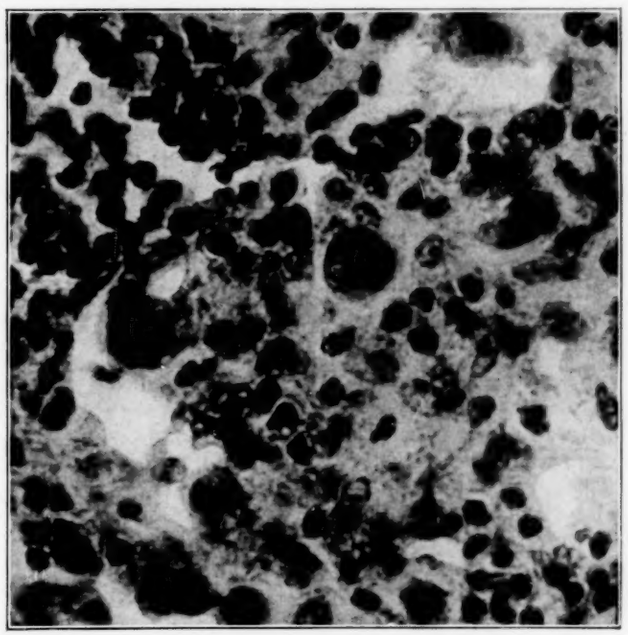

Fig. 4.—Reticulum cell lymphosarcoma with giant cells (× 900). Note the absence of fibrosis. This patient is alive and well six years after cervical dissection and postoperative roentgen therapy.

7a. Büngeler, W.: Die experimentelle Erzeugung von Leukämie, aleukämischen myelosen, Lymphadenosen und Lymphosarkom, Klin. Wchnschr. **11**: 1982 (Nov. 26) 1932.
7b. Gardner, W. U.: Estrogens in Carcinogenesis, Arch. Path. **27**: 138 (Jan.) 1939.
7c. Lewis, M. R.: Transplantable Lymphosarcoma in Mice, Am. J. Cancer **34**: 399 (Nov.) 1938.

7d. Anglem, Thomas: Unpublished Results of a Study of Hodgkin's Disease.

types of cancer, which at this clinic is 53.9 years.[7e] The age distribution in decades is very uniform, not more than 27 per cent of the total number falling within any single decennium (from 50 to 59 years, fig. 5). In general, lymphosarcoma is rare before the age of 20 years and after the age of 70 years. The youngest

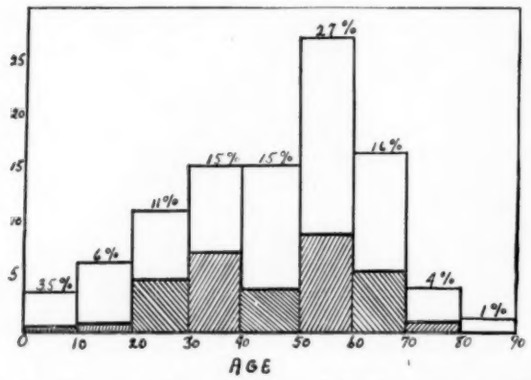

Fig. 5.—The sex and age incidence of lymphosarcoma according to decades, the average age and sex ratio. There were 138 males (white areas) and fifty-nine females (shaded areas), a ratio of 7 to 3. The average age for males was 45 years and for females 45.3 years.

patient was 4 years old and the oldest 88, and one of us has seen a proved case in a woman aged 107.

By far the largest number are of the reticulum cell type (184). Three cases were histologically diagnosed "malignant lymphocytoma" and nine cases presented the microscopic picture of giant follicle lymphoma (Brill-Symmers disease).

In comparison with other types of cancer (such as those of the breast, uterus and oral cavity), lymphosarcoma is not a common disease. The 196 cases here presented represent a collection of twenty years in an active metropolitan tumor clinic, an average of only ten cases a year. It must be reiterated, however, that these constitute only the number in which definitely positive biopsies were obtained but that there exist three other very definite groups: (1) that in which a single biopsy was suggestive but not definite, (2) that in which biopsy was impossible owing to inaccessibility of the disease and (3) that in which the necessary minor surgical procedure was refused by the patient. In each of these groups the subsequent clinical course was characteristic of a malignant lymphoma. Certainly, many of these patients had lymphosarcoma and therefore the figure just given must be taken to represent only an irreducible minimum.

CLINICAL FEATURES

In any disease such as this in which the possible sites of primary growth are not limited to any one organ or tissue but may occur almost anywhere within the body, and in which secondary dissemination eventually becomes widespread, it is obvious that any attempt at enumeration of clinical signs and symptoms would probably become so involved as to be of little practical value. However, it is possible by resorting to generalizations to obtain some information of real diagnostic worth.

Initial Symptom (fig. 6).—Visible and palpable external glandular swelling constituted the first evidence of disease in 65 per cent of the patients. The enlargement was in almost all cases entirely painless, though, in an occasional case in which there was massive swelling in the neck, pain traceable to infiltration of the cervical plexus was present. The amount of nodal swelling at the time of first examination varied considerably, from that which was hardly visible and barely palpable to masses producing gross physical deformity. Lymphosarcomatous nodes in general tend to have a characteristic resilient firmness not unlike that of uncured gum rubber. Usually the entire chain is involved, but exceptionally a solitary enlarged node may be present. They are more frequently discrete and movable until capsular invasion has taken place, when they tend to become matted together and fixed.

Symptoms referable to the abdomen occurred in 17.5 per cent of cases, and in two thirds of these the main complaint was pain of varying degree, usually little more than a vague discomfort but occasionally sharp and colicky, presumably due to interference with bowel function. Partial or complete intestinal obstruction, indefinite gastric complaints, melena, ascites and a dragging sensation in the abdomen make up the remainder. In 11.6 per cent difficulties of the upper respiratory tract were first complained of (such as sore throat, tonsillar swelling, nasal obstruction and bleeding). Thoracic symptoms were first to appear in only 3.6 per cent (pain, dyspnea, cough, upper mediastinal syndrome). Bone pain occurred initially in 1.83 per cent. Systemic symptoms (chill, fever, lassitude, increased sweating, weight loss) are conspicuously absent in early lymphosarcoma, rarely appearing until the disease has become far advanced.

The general mildness of the symptoms early in the disease is evidenced by the fact that the average duration of time from onset of symptoms to application for advice was 8.7 months.

Primary Site.—It has become traditional in many circles to consider lymphadenopathy in lymphosarcoma as a priori evidence of a primary site of disease in some other tissue or organ drained by the nodes involved. The usual sequence of events in carcinoma has probably given rise to this mental attitude.

In certain instances of rapidly disseminating disease it is impossible to determine whether a given organic

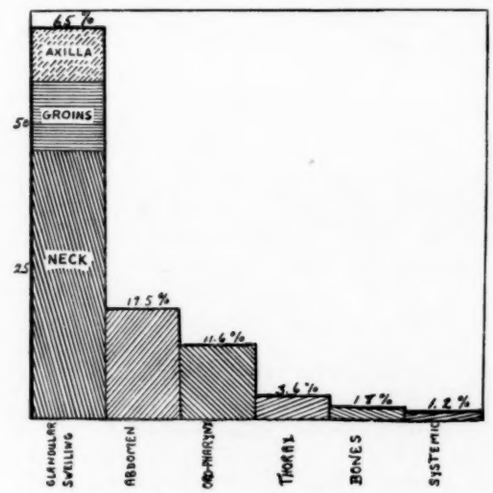

Fig. 6.—Anatomic distribution of the first sign or symptom indicative of disease.

involvement is primary or secondary. Exclusive of such cases, however, an extranodal focus of disease could be found and could reasonably be assumed to represent the primary site in only one third of the patients examined. In 65 per cent of these (table 1) the primary disease arose in one of the cranial structures with the tonsils and nasopharynx making up the majority. In 16 per cent it arose in the gastrointestinal tract

7e. Pack, G. T., and LeFevre, R. G.: The Age and Sex Distribution and Incidence of Neoplastic Diseases at the Memorial Hospital, City of New York, J. Cancer Research **14**: 167 (June) 1930.

(stomach six cases, jejunum two cases, ileum two cases, rectum one case). It is noteworthy that more than half of the gastrointestinal group arose in the stomach. Phillips and Kilgore [8] found, moreover, that thirty-nine of 100 histologically proved cases of gastric sarcoma were of the lymphoid type. In the remaining 19 per cent, primary sites were widely scattered (see recent report by Parker and Jackson [9]) : bone two cases, breast one case, skin of arm one case, lung one case, thymus two cases, prostate two cases, ovary one case, testicle three cases. It is interesting to observe that, though thymic lymphosarcoma is reported rather frequently, only two cases were present in this group. Two thirds of the entire series of patients never had what could reasonably be supposed to represent an extranodal primary focus. In these the first and only subsequent evidence of disease was confined to the node system until widespread dissemination took place. Moreover, many of the patients who have been free from disease for a number of years after receiving treatment to node groups alone never developed an extranodal primary focus which might earlier have remained concealed. It seems logical to suppose therefore that lymphosarcoma is a disease which in the majority of cases begins and

TABLE 1.—*Apparent Extranodal Primary Foci of Disease*

Site of Focus	Percentage		Site of Focus	Percentage
Tonsils	14	Head 22.5%	Bone	1
Nasopharynx	5		Prostate	1
Parotid	1		Testicle	1.5
Antrum	1		Ovary	0.5
Orbit	0.5		Breast	0.5
Eyelid	0.5		Lung	0.5
			Thymus	1
Stomach	3	Gastrointestinal 5.5%	Soft tissue of arm	0.5
Jejunum	1			
Ileum	1			
Rectum	0.5			

Total cases presenting an extranodal primary focus, 34.5%

runs its early course in lymph nodes alone. There is certainly no good reason for denying in these structures, the nodes, potentialities generally taken for granted in other mesenchymal derivatives.

The site of first node involvement is of considerable interest. In 59 per cent of the cases (table 2) this occurred in the neck (left forty-five, right thirty-seven, bilaterally twenty-two). The axilla was first involved in 11.4 per cent (left eight, right eleven, bilaterally one), the groins in 11.9 per cent (left ten, right nine, bilaterally two), the abdominal nodes in 13.1 per cent, the mediastinum in 1.1 per cent (surprisingly low) and the epitrochlear nodes in 0.5 per cent. In five cases (2.8 per cent) the disease appeared to involve almost the entire node system simultaneously.

Comparable figures for Hodgkin's disease at this hospital indicate the initial sites of node involvement to be neck 68 per cent, axilla 20 per cent, groins 12 per cent, mediastinum and abdomen 0 per cent.[7d]

Secondary Involvement.—In attempting to arrive at an arbitrary estimate of the extent of disease present on admission, cases were grouped according to the number of areas (not necessarily nodes) clinically involved. Because of recent extirpative surgery, 3.64 per cent had no clinical evidence of disease on admission. In 40.2 per cent there was only one area involved, in 12.5 per cent two contiguous areas contained disease, in 11.4 per cent three areas (not necessarily contiguous) were involved, and in 32.4 per cent more than three areas were involved and the disease was considered to be generalized. Only 24 per cent of the patients, therefore, had what might be termed intermediate stages of disease. It is questionable whether patients having three scattered areas of involvement might not be assumed

TABLE 2.—*Initial Node Group Involved*

Node Group	Right	Left	Bilateral	Total
Cervical	21 %	25.6%	12.5%	59.1%
Axillary	6.3%	4.5%	0.6%	11.4%
Groin	5.1%	5.7%	1.1%	11.9%
Abdomen				13.1%
Mediastinum				1.1%
Epitrochlear				5 %
Generalized				2.8%

to have generalized disease, which, if true, would reduce the intermediate group to 12.5 per cent. In view of only slight differences in the duration of symptoms prior to admission in each of these groups, the smallness of the intermediate group stands as incontrovertible evidence of the rapidity with which the disease advances once it has broken away from the primary site. Indeed, in particular instances untreated disease which had remained apparently static for several years would suddenly or in a few months become widely disseminated.

In general, lymphosarcoma is an acutely malignant disease. Chronic forms do occur but constitute a small minority. In no other disease is metastasis apt to be so sudden and widespread. Hardly an organ or tissue is spared. Lymph node involvement eventually occurs in 100 per cent of cases unless death due to gastric hemorrhage, intestinal obstruction or some unrelated cause suddenly terminates the course of the disease. At first the disease is largely confined to the lymphatic system, contiguous node groups being successively affected; more rarely, widely separate node groups may become involved in rapid sequence or even simultaneously.

In addition to the primary sites of involvement, intranodal or extranodal, numerous organs may subsequently become involved either as a result of lymphatic or hematogenous metastasis or by direct extension (table 3).

TABLE 3.—*Organs Clinically Involved Later in the Course of the Disease, Presumably as a Result of Hematogenous or Lymphogenous Spread*

Site of Involvement	Percentage	Site of Involvement	Percentage
Spleen	21	Bladder	1.0
Lungs	12	Penis	0.5
Bones	9.7	Ethmoids	0.5
Liver	8	Brain	0.5
Skin	5.5	Larynx	0.5
Intestinal tract	5	Lacrimal gland	0.5
Tonsils	5	Orbit	0.5
Stomach	2	Conjunctiva	0.5
Testes	1.5	Tongue	0.5
Spinal cord	1.5	Palate	0.5
Breast	1.0		

The spleen was palpable in 21 per cent of cases, though rarely was it greatly enlarged unless lymphatic leukemia became superimposed. Liver involvement as evidenced by a palpably enlarged organ was noted in only 8 per cent. There was roentgenographic evidence of pleuropulmonary infiltration in 12 per cent of cases as manifested by lung mottling or pleural effusion. X-ray evidence [9a] of secondary bone involvement was present

8. Phillips, J. R., and Kilgore, F. H.: Lymphosarcoma of the Stomach, Am. J. Surg. **31**: 179 (Jan.) 1936.
9. Parker, Frederic, Jr., and Jackson, Henry, Jr.: Primary Reticulum Cell Sarcoma of Bone, Surg., Gynec. & Obst. **68**: 45 (Jan.) 1939.

9a. Craver, L. F., and Copeland, M. M.: Lymphosarcoma in Bone, Arch. Surg. **28**: 809 (May) 1934.

in 9.1 per cent. Undoubtedly this figure is too low. Comparative figures obtained by Anglem for Hodgkin's disease indicate the presence of a palpable spleen in 45 per cent, of a palpably enlarged liver in 24 per cent, of lung involvement in 29 per cent and of bone involvement in 24 per cent. Boring pain, the usual symptom of

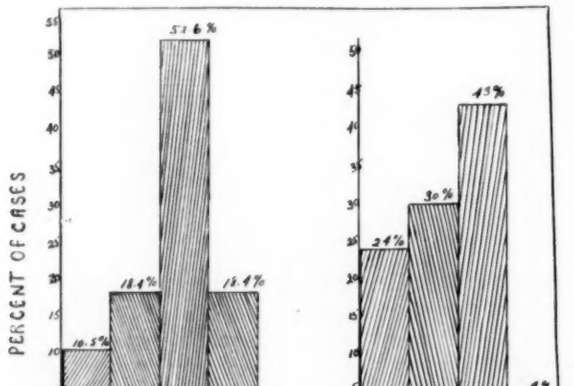

Fig. 7.—The hemoglobin percentage on admission (left) and within six months to one week before death (right).

metastatic bone disease, is far more common in lymphosarcoma than the just mentioned figure of 9.1 per cent would indicate, and many of these patients with bone pain never present any roentgenographic evidence of osseous disease, presumably because the lesion is too small to cast a shadow or because there is insufficient bone reaction to its presence. Treatment becomes mandatory to relieve the pain and usually accomplishes this very nicely, but the possibility of ever obtaining evidence of the disease in the bone may thereby be destroyed. The large bones are more frequently involved (spine, pelvis, skull and long bones) probably because of their proportionately greater blood supply, since secondary lymphosarcoma of bone is largely a manifestation of

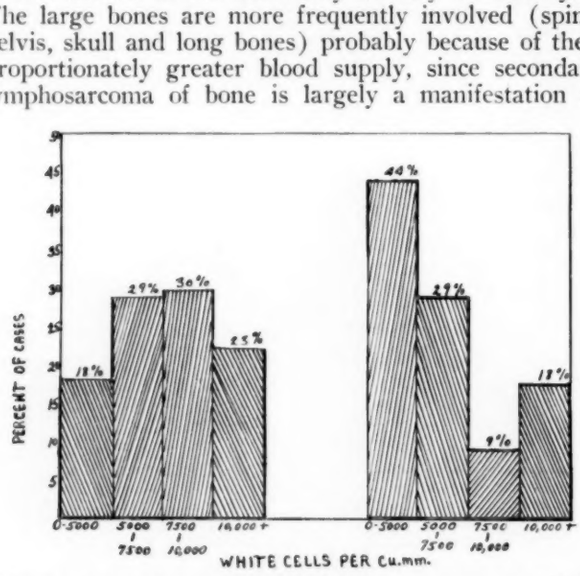

Fig. 8.—A comparison of the total white blood cell count on admission (left) and within six months to one week before death (right).

hematogenous spread. Metastatic involvement of the skin occurs in about 5.5 per cent of cases. Intracutaneous nodules are usually quite firm but lack the hard consistency of carcinomatous nodules and usually have a shiny bluish red appearance. Evidence of presumably secondary gastrointestinal involvement was obtained in 5.5 per cent. In none of these was the duodenum involved. Other organs which later became involved in occasional instances were tonsils five, testis three, breast two, ethmoid sinus one, lacrimal gland one, orbit one, conjunctiva one, palate one, larynx one, bladder two, penis one, spinal cord three, brain one. In cases presenting evidence of hematogenous spread[9b] (as in lungs, bones, skin and spleen) the prognosis is extremely bad and the life expectancy is apt to be very short. The rapidity with which lymphosarcoma advances is readily understood when one considers that the average duration of life from onset of disease till death was 20.5 months.

Hemogram.—There is no specific hemogram in lymphosarcoma. Early in the course of the disease and for some time after its onset, the blood picture remains amazingly cheering. In contradistinction to patients with Hodgkin's disease, in whom anemia usually develops early (32 per cent on admission), lymphosarcoma patients maintain excellent hemoglobin values for some time (fig. 7). On admission 70 per cent of the patients showed hemoglobin readings above 80 per cent and only 10 per cent of patients less than 70 per cent.

The total white cell count (fig. 8) on admission was above 7,500 in 53 per cent of cases. Twenty-three per cent showed leukocytosis with a count above 10,000.

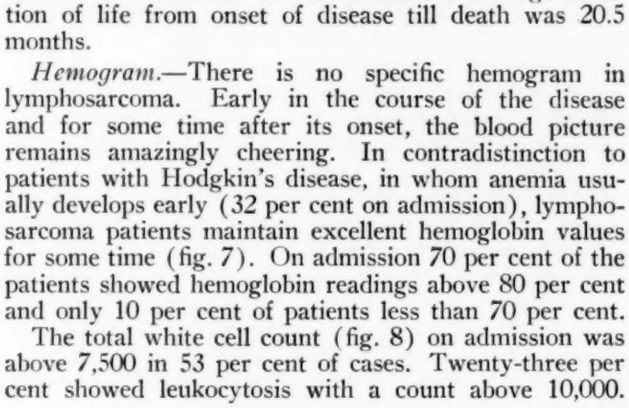

Fig. 9.—Predominance of the granulocytic cells in the blood smear throughout the course of lymphosarcoma; left, on admission; right, six months to one week before death.

Eighteen per cent had less than 5,000 white cells per cubic millimeter of blood. Cells of the granulocytic series predominated. In 82 per cent of patients (fig. 9) they exceeded 60 per cent and in 31 per cent of the cases the granulocytes exceeded 80 per cent of the total count (definite polycytosis). The lymphocytic cells were, of course, in inverse ratio.

As a result of advancing disease combined with radiation therapy, very definite blood cell changes took place as indicated by counts taken from six months to several days before death. The most important of these changes was anemia. At this time only 46 per cent of cases showed hemoglobin percentages above 80, whereas 24 per cent read less than 70. The total white count dropped to less than 5,000 in 44 per cent and only 27 per cent had more than 7,000 per cubic millimeter. Accompanying this there was little discernible change in the differential count, the granulocytes remaining up. Thirteen patients (6.6 per cent) presented a leukemic or definitely pseudoleukemic blood picture, all of the lymphocytic type.[9c] Twelve of these had been histo-

9b. Klemperer, Paul: The Spleen in Hodgkin's Disease, Lymphosarcomatosis and Leukemia, Am. J. M. Sc. **188**: 593 (Nov.) 1934.

9c. Craver, L. F.: Clinical Manifestations and Treatment of Leukemia, Am. J. Cancer **26**: 124 (Jan.) 1936; Five Year Survivals in Lymphatic Tumors, Surg., Gynec. & Obst. **60**: 485 (Feb.) 1935; Hodgkin's Disease, Lymphosarcoma and Leukemia, Laryngoscope **43**: 575 (July) 1933.

logically diagnosed as reticulum cell lymphosarcoma and one as giant follicular lymphoma. In none of the three cases of malignant lymphocytoma was this complication noted.

DIFFERENTIAL DIAGNOSIS

Experience in clinical observation of the lymphomas teaches caution in attempting differential diagnosis except by an excisional biopsy interpreted by a skilled pathologist. In general the best one can do clinically is to hazard a guess, which at times may have to include two, three or more possible diagnoses. There are no clinical features which without exception will permit a differentiation between tuberculous lymphadenitis, Hodgkin's disease, lymphosarcoma, aleukemic lymphatic leukemia, lympho-epithelioma, or even metastatic carcinoma in lymph nodes. The application of a therapeutic test dose of radiation is of little diagnostic value, as any of the first mentioned conditions may respond as readily as does lymphosarcoma.

As clinically observed, lymphosarcomas may be roughly divided into two groups: those with a process obviously of monocentric origin, presenting an asymmetrical lymphadenopathy, bulking mainly in one to a few groups of nodes; and those, perhaps of multicentric origin, presenting a fairly uniform symmetrical distribution of nodes, at once suggesting chronic lymphatic leukemia. In the latter group a nonleukemic blood count necessitates a lymph node biopsy to distinguish between generalized Hodgkin's disease, rare cases of metastatic carcinoma, and especially between aleukemic leukemia and lymphosarcoma (if it is proper to make the latter distinction). Moreover, leukemic blood does not necessarily exclude lymphosarcoma. There are also rare cases of generalized symmetrical tuberculous lymphadenitis and other generalized adenopathies of inflammatory or metabolic origin.

Concerning the former more localized types, it may be said in general that lymphosarcoma tends to be more diffuse and more aggressive than the other processes mentioned. The nodes in lymphosarcoma tend to assume a rounded shape and a rubbery firm consistency.

The rare diffuse lymphosarcoma of the nasopharyngeal and oropharyngeal tonsillar ring presents a characteristic appearance. Lymphosarcoma of the tonsil, when fully developed, usually presents a bulky smooth spongy swelling in the tonsillar fossa with little or no ulceration until late stages. Lymphosarcoma of the stomach, like lymphatic leukemia, may produce giant rugae. In the intestine, lymphosarcoma may produce a bulky palpable mass with comparatively little stenosis of the lumen. In the skin, lymphosarcoma characteristically causes raised, dusky red button-like plaques, similar to leukemia cutis.

(To be continued)

Education of Adult Blind.—In the United States there are 27,872 blind persons between the ages of 25 and 64 years, and 28,113 of over 64 years, according to the 1930 federal census. The National Health Survey of 1935-1936 estimates that there are 76,000 blind persons of over 55 years of age, 33,000 of between 25 and 55 years. The average age of the blind is just over 60 years; 78.7 per cent of the blind are over 45 years of age. Only 45.9 per cent of these blind persons have ever attended school. . . . About 8,000 blind persons in the United States are taught by home teachers, and there is an average of one teacher to every 100 persons taught.—Education of the Handicapped, edited by M. E. Frampton and H. G. Rowell, Yonkers-on-Hudson, New York, 1940, vol. 2, p. 150.

ORAL POLLEN THERAPY IN RAGWEED POLLINOSIS

A COOPERATIVE STUDY

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The progress made in the last few years in the various phases of immunotherapy has stimulated the search for more simple methods for the administration of such treatment. Attempts at substitution of the oral method for the hypodermic type in vaccine and allergen administration were begun many years ago. Among the first clinical conditions for which prophylaxis by ingestion was suggested is hay fever. The hope of safety, convenience, inexpensiveness and painlessness of the oral method has been the motivating factor stimulating this idea.

In 1900, more than ten years prior to the advocation of hypodermic pollen therapy, Curtis [1] had recommended the oral administration of extracts of ragweed pollen. He had previously observed the good effects of infusions of roses and other flowers in those sensitive to them. The patients were given, three times daily after each meal, from 2 to 10 drops of a tincture or infusion of the flowers and pollen of ragweed. For most patients the treatment was begun two weeks prior to the season and continued through the season. For some it was used coseasonally only. With both methods of treatment good results were obtained in the majority of cases.

Strangely enough, for the next twenty years or more, the possibilities inherent in such therapy seemed to have been ignored. In 1922 Touart [2] described the results that were obtained from treating six patients with daily doses of 0.1 mg. pollen tablets coated with phenyl salicylate. The grass-sensitive patient obtained relief, while only one of those allergic to ragweed pollen was benefited.

Black in 1927 [3] and 1928 [4] reported on his results with oral pollen therapy. While he obtained complete failures in 6 per cent of hay fever cases treated hypodermically, the failures with the oral method amounted to 20 per cent. In the cases of pollen asthma, complete failures resulted in 22.2 per cent with oral treatment, while with the hypodermic method no complete failures occurred. Thommen [5] has reported the successful oral

The pollen and placebo capsules for this study were obtained through Eli Lilly & Co., Indianapolis. This product has not been considered by the Council on Pharmacy and Chemistry of the American Medical Association.

1. Curtis, H. H.: The Immunizing Cure of Hay Fever, M. News, New York **77**: 16, 1900.
2. Touart, M. D.: Hay Fever: Desensitization by Ingestion of Pollen Proteins, New York M. J. **116**: 199 (Aug. 16) 1922.
3. Black, J. H.: The Oral Administration of Pollen, J. Lab. & Clin. Med. **12**: 1156 (Sept.) 1927.
4. Black, J. H.: The Oral Administration of Pollen: A Clinical Report, J. Lab. & Clin. Med. **13**: 709 (May) 1928.
5. Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, Publisher, 1931, p. 764.

pollen treatment of one hay fever patient, but his experiences with later cases were disappointing. Urbach [6] for a number of years has been advocating specific oral pollen peptone therapy.

Gatterdam [7] in 1933 and 1934 recommended this type of treatment on the basis of his report, describing good results in from 75 to 85 per cent of a series of eighty-five patients. The author administered from 3 to 15 drops of a 3 per cent pollen extract twice daily, with additional doses during attacks. The pollens employed were those of cottonwood, ash, Bermuda grass, rabbit bush and false ragweeds. McGrew [8] tried oral pollen therapy on the basis that he had known some hay fever sufferers to claim relief by the ingestion of honey and that the pollen in the honey might be responsible for this action. Coseasonal treatment was given, using from 1 to 10 drops of a 1 per cent extract three times daily for the immediate relief of an individual attack. Of thirty-three patients, twenty-nine were improved. Those having asthma did not do as well.

Despite the reports just cited, it was not until the work of Stier and Hollister [9] became known that this subject began to arouse general interest. In an experience extending over three years these authors obtained satisfactory results in 78 per cent of a large series of hay fever cases. Their best results were obtained with the coseasonal method. The doses varied from 3 drops of a 1:100,000 dilution to a maximum dose of 21 drops of a 1:100 dilution (from 2 to 14,000 pollen units). A large variety of pollen was used but, because their region does not contain ragweed, it did not include an evaluation of oral ragweed therapy.

Rockwell [10] in 1938 reported on his results in a series of hay fever cases treated during the years from 1935 to 1937 inclusive. His methods differed somewhat each year, but his latest method was the use of dry ground pollen in capsules. Beginning with 500 pollen units (0.5 mg.) the doses were increased to 120,000 or 240,000 (120 to 240 mg.). Preseasonal doses were given twice weekly and the seasonal doses several times weekly. In coseasonal treatment the capsules were given three times daily at first. The coseasonal therapy yielded the best results, satisfactory relief occurring in 75 per cent of his cases.

Bohner,[11] employing the same technic as Rockwell, obtained less happy results. Of twenty-one patients, thirteen obtained satisfactory benefit while of an equal number treated hypodermically sixteen were benefited. In the same year Bernstein and Feinberg [12] analyzed the results in twenty ragweed-sensitive patients treated with pollen orally during the 1937 season. Pollen extract, well diluted, in doses from 6,000 to 180,000 pollen units, were administered daily. All patients were treated coseasonally. Only two obtained some degree of relief.

Recently Black [13] reported a reinvestigation of the oral method during the 1938 season in Dallas. Of forty patients treated with daily doses of 500 to 4,000 units, sixteen (40 per cent) obtained satisfactory relief. Black makes the observation that in some instances oral pollen therapy was of aid as adjunct treatment in overcoming the tendency of the individual to repeated systemic reactions from the hypodermic injection of the extract. London [14] investigated the combined effect of hypodermic and oral pollen therapy. He concludes that patients adequately treated by the subcutaneous method can expect no further benefit from the supplementary oral administration of pollen.

Of twenty-two ragweed patients treated preseasonally by Zeller [15] during 1938 with pollen given orally, 20 per cent obtained good results. Of the five who obtained good results two had had from three to four years of good results previously with hypodermic therapy. The simultaneous administration of the oral pollen and hypodermic treatment did not improve the results of the latter treatment. In the discussion of Zeller's paper,[15] Vaughan mentioned that he obtained relief by the oral method in from 10 to 20 per cent of his cases. Ellis obtained complete failures in fourteen out of fifteen cases. Bernton recalled that fifteen years previously he treated thirty hay fever patients with pollen tablets with complete failure in all. Bohner cited statistics less favorable than he had reported previously.

Most of the papers report a fairly high incidence of gastrointestinal reactions. For instance, Bernstein and Feinberg [12] report an incidence of 30 per cent, Zeller [15] an incidence of over 40 per cent. There is much less certainty concerning constitutional allergic reactions such as urticaria, hay fever or asthma. If they occur they are uncommon. This observation provokes the question of absorption of the pollen administered orally. Black [3] found that the ragweed atopen could be demonstrated in the blood and urine after the ingestion of large amounts of pollen extract. The basis for his conclusion was the observation of positive intracutaneous tests with such blood serum in ragweed-sensitive persons and in those passively sensitized. Clarence Bernstein Jr. and Kirsner [16] were unable to demonstrate enteral absorption from a 0.3 Gm. capsule of ragweed pollen sufficient to cause a reaction in passively sensitized sites in four persons. Using similar methods T. B. Bernstein and Feinberg [12] tested enteral absorption of ragweed pollen in seventeen nonallergic subjects. In sixteen no reactions were obtained, although doses as high as 5 Gm. (5,000,000 pollen units) were administered. In one person with a bleeding carcinoma of the stomach, evidence of absorption was obtained. It is interesting to note that in all of these seventeen persons the hypodermic administration of pollen extract showed reactions in the distantly sensitized sites with amounts as little as one five-thousandth part of that used orally. Zeller [15] and London [14] independently confirmed these observations by employing a combination of the methods used by Bernstein and Feinberg with those of Black.

6. Urbach, Erich: Desensibilisierung pollen allergischer Individuen auf oralem Wege mittels artspezifischer Pollenpeptone, Klin. Wchnschr. **10:** 534 (March 21) 1931; Die Behandlung des Heufiebers mittels artspezifischer Gräserblüten-Propeptone bzw. Pollen-Mikromahlzeiten, ibid. **12:** 1797 (Nov. 18) 1933; Pathogenese und Therapie des Heufiebers, Wien. Klin. Wchnschr. **47:** 1073 (Aug. 31) 1934; Die biologische Behandlung des Heufiebers, München. med. Wchnschr. **84:** 488 (March 26) 1937.

7. Gatterdam, E. A.: Oral Administration of Pollen Extracts, Southwest Med. **17:** 199 (June) 1933; Hay Fever in Central Arizona and Its Treatment with Oral Extracts, ibid. **18:** 130 (April) 1934.

8. McGrew, G. D.: Time and Money Saved in the Treatment of Hay Fever, Mil. Surgeon **80:** 371 (May) 1937.

9. Stier, R. F. E., and Hollister, Guy: Desensitization by Oral Administration of Pollen Extracts, Northwest Med. **36:** 166 (May) 1937.

10. Rockwell, G. E.: Clinical Results in the Prevention and Treatment of Hay Fever by Oral Administration of Pollens of the Grass and Ragweed Types, Ohio State M. J. **34:** 784 (July) 1938.

11. Bohner, C. B.: Treatment of Ragweed Pollinosis: Comparison of Oral and Hypodermic Medication, J. Indiana M. A. **31:** 279 (June) 1938.

12. Bernstein, T. B., and Feinberg, S. M.: Oral Ragweed Pollen Therapy: Clinical Results and Experiments on Gastrointestinal Absorption, Arch. Int. Med. **62:** 297 (Aug.) 1938.

13. Black, J. H.: The Oral Administration of Ragweed Pollen, J. Allergy **10:** 156 (Jan.) 1939.

14. London, McKinley: Combined Oral and Subcutaneous Treatment for Ragweed Pollinosis, J. Allergy **10:** 453 (July) 1939.

15. Zeller, Michael: Oral Ragweed Pollen Therapy (with discussion), J. Allergy **10:** 579 (Sept.) 1939.

16. Bernstein, Clarence, Jr., and Kirsner, J. B.: Oral Pollen Therapy, J. Allergy **8:** 221 (March) 1937.

The somewhat conflicting results of the published reports and the potential importance of such a method of therapy stimulated several of us connected with the allergy clinics at the University of Illinois College of Medicine, Northwestern University Medical School, Rush Medical College, University of Chicago and the University of Michigan Medical School to plan a cooperative project in the summer of 1939, in order to evaluate oral pollen therapy. It was planned that the several institutions would proceed with their own work and observations with slight individual variations, but that each would follow the same general plan herein described.

The patients selected were those who had ragweed hay fever or hay fever and asthma and either had never been treated hypodermically or at least had had no treatment later than 1937. This was done to eliminate the possible residual benefit obtained from previous hypodermic therapy. The materials administered to the patients were capsules containing differing amounts of dry pollen diluted with starch. The capsules of varying content were of different colors for the sake of identification. Identically colored capsules containing starch only were available for placebo purposes. The majority of the patients selected for the experiment received the pollen capsules together with an injection of physiologic solution of sodium chloride.

Those treated preseasonally were instructed to take single doses twice weekly, beginning with 500 pollen units and doubling each dose until the level of about 180,000 units was reached. When patients reported after mid-July the intervals were shortened in order to reach the maximum dose before August 15. During the season instructions were given to take the capsules once daily. A few divided their daily portions into two or three doses. Those who began their treatment during the season were instructed to take the pollen three times daily. The capsules were usually administered after meals.

Before treatment was started, all the investigators used a uniform questionnaire eliciting specific data as to the severity and character of each patient's past seasons, especially the 1938 season as the one most recently in memory. The information thus obtained was the yardstick for comparison of results in the 1939 season.

After pollination began the patients were questioned and observed as to the frequency and severity of symptoms, and written notations were made. Every attempt was made to elicit objective data, such as loss of sleep and interruption of work, as well as the patient's own estimate of symptoms. Discrepancies between the patient's report and our own observations were usually reconciled by a cross examination of the patient or his relatives. If the patient failed to report weekly, the social service department investigated by telephone or letter; this cooperation made a very complete follow-up study possible.

RAGWEED ORAL POLLEN THERAPY COMPARED WITH ORAL PLACEBO[17]

By Drs. Ben Z. Rappaport, Michael Zeller and Emanuel Padnos

The main group in this study consisted of 103 subjects varying in age from 6 to 73 years. Fifteen of these were children under 14 years. Sixty-four had uncomplicated autumnal hay fever, while thirty-nine had fall pollen asthma. (In addition to this group of 103, one of us [E. P.] studied twelve children, whose cases will be discussed under a separate heading.) All had positive cutaneous reactions to the ragweed pollens. Seventy-one of the group, consisting of the thirty-nine patients with asthma and thirty-two with hay fever, were given ragweed pollen orally. The remaining thirty-two, all with uncomplicated hay fever, were given placebo capsules which were identical in color and appearance with the oral pollen capsules. It was not considered justifiable to include patients with asthma in the placebo group. In addition to the pollen or placebo capsules, each patient received a subcutaneous injection of physiologic solution of sodium chloride on reporting to the clinic once a week.

DOSAGE

The initial oral dose of ragweed pollen varied from 1,000 to 2,000 units. This dose was increased by doubling the previous dose twice a week for those patients who reported early for treatment. Only eight of the patients came after July 1. The dose in this small group was given more frequently to attain a comparable maximum pollen dose. The maximum dose attained was 60,000 units by thirteen patients, 120,000 units by thirty-three, 180,000 units by nineteen and 240,000 units by two. This was attained with no untoward symptoms by thirty-six of the seventy-one patients several weeks before the onset of the hay fever symptoms. It was maintained at the level planned in spite of the fact that an increase in dose could easily have been given to most of the patients. With the onset of symptoms during the first ten days of August the maximum preseasonal dose was given daily. It was, however, varied from day to day, being increased in most cases in an attempt to control symptoms.

The total amount of pollen ingested during the course of treatment varied even more than the maximum dosage. Three patients received between 1 and 2 million Noon units, twenty-six between 2 and 4 million, nine between 4 and 6 million, nineteen between 6 and 10 million, twenty-two between 10 and 15 million and two patients more than 15 million.

UNTOWARD EFFECTS OF ORAL POLLEN

The untoward effects of treatment consisted principally of gastrointestinal symptoms such as abdominal cramps, nausea, vomiting and diarrhea. In some patients these symptoms manifested themselves after each individual dose, while in others they developed at irregular intervals without any apparent relationship to dosage. Gastrointestinal symptoms were usually noted within one half hour to two hours after ingestion of the capsules and persisted for periods varying from one to thirty-six hours. In some instances reduction of dosage or abstinence from oral pollen apparently increased gastrointestinal tolerance to a point where continued treatment was possible without untoward reactions.

Four patients started on oral therapy and not included in the group of 103 previously discussed had violent abdominal pain and diarrhea and refused further treatment before the onset of the hay fever season.

Hay fever after oral pollen occurred in eleven cases, but in no instance was it severe, and it usually subsided within one hour. Other possible sources of nasal symptoms were ruled out before considering oral pollen as

17. From the Allergy Clinic of the Departments of Medicine and Pediatrics, University of Illinois College of Medicine.

the cause. In one case asthma followed the initial oral pollen dose on repeated trials. Further therapy was, therefore, not practical. In one other instance asthma occurred several times after ingestion of 120,000 units, but on reduction of the dose further difficulty was avoided. Three patients had headache, drowsiness and dizziness. Urticaria was not observed in any instance.

These observations as well as those to be discussed in the reports of our collaborators indicate that the majority of the untoward reactions are limited to the gastrointestinal tract. The effect of a large initial dose, however, produced no untoward effect in any of the patients to whom it was given. Five of the patients who had asthma were given 30,000 ragweed pollen units one hour after a heavy meal as the initial preseasonal dose. No gastrointestinal or other symptoms followed this. Ten of the thirty-two patients placed on placebo treatment were likewise given a large initial dose of ragweed pollen before receiving the placebo capsules. Five of the ten were given 30,000 pollen units while the other five received 60,000 pollen units. No gastrointestinal or other symptoms occurred in any of these patients.

TABLE 1.—*Summary and Comparison of Results in 103 Ragweed-Sensitive Patients Treated by Oral Pollen and by Oral Placebo at the University of Illinois College of Medicine*

			Degree of Improvement			
	Unimproved	Improved	Slight	Moderate	Good	Excellent
Asthma (oral pollen)....	32 (82%)	7 (18%)	0	5 (12.8%)	2 (5.2%)	0
Hay fever (oral pollen)....	20 (62.5%)	12 (37.5%)	6 (18.75%)	3 (9.37%)	3 (9.37%)	0
Hay fever (oral placebo)..	25 (78.1%)	7 (21.9%)	1 (3.1%)	4 (12.5%)	0	2 (6.25%)

RESULTS

The results of treatment are briefly indicated in table 1. In more detailed protocols attempts were made to determine whether improvement in each case was slight, moderate, good or excellent. These have been condensed in table 1.

It will be noted that of the thirty-two patients with uncomplicated hay fever twenty (62 per cent) showed no improvement. Six were slightly improved and six showed moderate (50 per cent) to good (75 per cent) improvement.

The thirty-nine asthma patients may be grouped into two classes, thirty-two (82 per cent) with no improvement and seven (18 per cent) with moderate to good results. None were completely or nearly completely relieved. Of the thirty-two who were unimproved, five had asthma as severe as in the previous untreated year while fourteen stated that their condition was worse.

Fifteen of this group of 103 patients were children aged 6 to 14. Seven of the fifteen had autumnal asthma; none of these showed any improvement. Eight of the fifteen had simple autumnal hay fever; six were unimproved while two had slight improvement. Three of these fifteen had a maximum oral pollen dose of 60,000 units. The rest reached a dose of from 120,000 to 180,000 units. These patients were studied by two of us (B. Z. R. and M. Z.).

A group of twelve children ranging in age from 7 to 15 years was studied separately by one of us (E. P.). The results in this group were so different that the subjects are described separately and were not included among the 103 patients previously discussed. Nine of these patients had simple autumnal hay fever, while three had autumnal asthma. Eleven of the twelve received ragweed pollen orally while the twelfth received placebo capsules. Five other placebo-treated patients of the group discontinued treatment before the beginning of the hay fever season. The maximum dose attained was 120,000 pollen units by one, 180,000 units by three, 240,000 units by one, 360,000 units by three and 420,000 units by three. No untoward symptoms occurred in any of the patients.

The parents as well as the children were questioned regarding the results obtained. Eight of the nine hay fever patients receiving oral pollen claimed improvement—with the following estimates of the degree of relief: one very slight, two moderate, four good and one excellent. The three patients with autumnal asthma were all moderately improved. The one patient receiving placebo capsules was also moderately improved. According to the results obtained in this group, all patients, the three with asthma and the nine with hay fever, including the one patient receiving placebo therapy, had moderate to marked improvement.

PLACEBO GROUP

The surprise of the experiment came in tabulating the results of the oral placebo group. Great care had been taken to treat and question these thirty-two patients in the same manner as those receiving pollen orally. Seven of the group (21.9 per cent) stated that they were improved, while twenty-five (78.1 per cent) were unimproved. Of the seven who were improved by the placebo capsules and saline injections, six (18.75 per cent) had more than moderate relief. Two of these six had results classified as excellent, an apparently better result than that obtained by any of the patients receiving oral pollen therapy.

COMMENT

The interesting comparison in this study is in the results of the thirty-two patients with simple hay fever given pollen orally and the equal number given placebo capsules orally. Of those receiving pollen orally, six were slightly improved and six had moderate to good results. In the oral placebo group only one was slightly improved, while six had moderate to excellent results. The similarity of these results is striking. Unfortunately, the number of patients in both groups is too small for any definite conclusions to be drawn.

On the other hand, when one compares the results obtained in the two groups of children studied, no good explanation can be offered for the discrepancies shown. In the fifteen patients under 14 years studied by two of us (B. Z. R. and M. Z.) only two had slight improvement. All of the twelve children studied by one of us (E. P.), including the one given a placebo, reported improvement. This report was confirmed by the parents. Only one of this uniformly favorable group reported slight (questionable) improvement. It will be noted that seven of the eleven in this latter group received a maximum dose of from 240,000 to 420,000 pollen units. This is definitely a much higher dose than that received by the other group of fifteen children. We are uncertain whether this accounts for the difference in results reported or whether it is largely a difference of interpretation by different observers.

SUMMARY

1. In this study, thirty-two patients with uncomplicated ragweed hay fever were given pollen orally, while an equal number received placebo capsules.

2. Of the thirty-nine patients with asthma who received pollen orally, seven (18 per cent) stated that they had moderate to good results. None were completely relieved. The remainder (82 per cent) were unimproved. Of the thirty-two patients with uncomplicated hay fever receiving pollen orally, six (18.75 per cent) were slightly improved and six (18.75 per cent) had moderate to good results; of the thirty-two receiving placebo capsules orally, one (3.1 per cent) was slightly improved while six (18.75 per cent) had moderate to excellent results. Therefore the results for subjects with uncomplicated hay fever treated with oral pollen show no substantial difference from results for those receiving placebo capsules.

3. Two groups of children studied by different observers show conflicting results. In one group, eleven patients receiving oral pollen reported uniformly favorable results. In the other group of fifteen receiving oral pollen, only two reported slight improvement.

COMPARISON OF ORAL POLLEN WITH PARENTERAL POLLEN IN THE TREATMENT OF RAGWEED POLLINOSIS [18]

BY DRS. FRANCIS L. FORAN AND MEYER R. LICHTENSTEIN

Two groups were observed in this series, each reporting to the clinic on an average of once a week. The "oral pollen group" of thirty-two patients received on each visit an injection of physiologic solution of sodium chloride and a sufficient number of pollen capsules with a written dosage schedule for the ensuing week. The "parenteral pollen group" of twenty-five patients received on each visit an injection of pollen extract and a number of placebo capsules, also with written directions and dosages for the ensuing week.

None of the fifty-seven patients used in this study had received treatment in 1938. Of the oral group eleven had received parenteral injections in some years previous to 1938; of the parenteral group six had received such treatment previous to 1938. Only two patients in the entire series were under 16 years of age; otherwise the ages ranged from 16 to 72.

Throughout the study care was taken to make the same inquiries of both groups as to symptoms and reactions in order to equalize as far as possible the psychologic factors. Thus patients of both groups were asked in a routine way about local reactions from the injections. The saline injections occasionally gave slight discomfort, enough to rationalize the inquiry to the patient receiving them. Again, to avoid leading questions, we made no inquiry about gastrointestinal reactions until a complaint was volunteered.

TREATMENT AND DOSAGE

Treatment was begun during May in all but six cases and continued into the first week of September or later with only two exceptions, the two subjects refusing further treatment because of severe gastrointestinal reactions.

The range of dosage is summarized in table 2, items D, E and F. In averaging the number of doses and the maximum daily dose the entire daily intake is counted as one dose, although many patients split the amount into two or more fractions, usually because of gastrointestinal discomfort with the larger amount. The total course dose is the sum expressed in Noon units of all the pollen ingested or injected during the entire course of treatment.

It is pertinent to compare the ratio of doses used in the two groups. The average maximum daily dose of the oral pollen was approximately fifty times that of the parenteral pollen extract (table 2, item E) and the average total pollen ingested throughout the entire course of treatment was approximately two hundred times that injected in the parenteral group (table 2, item F).

REACTIONS

Eight (25 per cent) of the oral group had gastrointestinal reactions such as epigastric pain, cramps, nausea, vomiting or diarrhea. In three patients the symptoms were of repeated occurrence and one of them finally refused further treatment on August 26. Still another, a medical student, discontinued treatment on August 26 after severe nausea and diarrhea, although the pollen had been fairly well tolerated to that time. The other patients with gastrointestinal symptoms were readily relieved by reducing or fractionating the dose.

Two patients complained of urticaria and two of pruritus, both symptoms being of minor severity and of brief duration. One patient only spoke of "choking" after 90,000 units, but no definite asthma syndrome seemed to have occurred.

No systemic reactions occurred in the parenterally treated group, owing probably to the conservative dosage schedule followed.

TABLE 2.—*Summary of Study of Oral Pollen Therapy. Rush Medical College, University of Chicago*

Type of Cases	Oral Group *	Parenteral Group †
A. Total number of cases	32	25
B. In 1938, hay fever only	18	10
C. In 1938, hay fever and asthma	14 (44% of A)	15 (60% of A)
Treatment in 1939 Season		
D. Average number of doses	40	14.4
Variation	(23-62)	(7-21)
E. Average maximum daily dose	116,000	2,452
Variation	(60,000-120,000)	(700-4,500)
F. Average total course dose	3,237,000	16,817
Variation	(675,000-5,113,000)	(1,930-41,320)
Results of Treatment		
G. In 1939, hay fever only	10	10
H. In 1939, hay fever and asthma	22 (69% of A)	15 (60% of A)
I. In 1939, asthma for first time	9 (50% of B)	2 (20% of B)
Comparison with 1938 Season		
J. Symptoms same	3 (10%)	7 (28%)
K. Symptoms better	8 (25%)	14 (56%)
L. Symptoms worse	21 (65%)	4 (16%)

* Received oral pollen and saline injections.
† Received pollen extract injections and placebo capsules.

RESULTS

It should be remarked that the 1939 season was more severe in the Chicago area than that of 1938 and therefore the mere fact of aggravation of symptoms does not preclude some effectiveness of the therapeutic agent employed. However, a comparative estimate of the experimental and control groups is a fair and reasonable ground for conclusions.

18. From the Allergy Clinic, Rush Medical College, University of Chicago.

The characterization of results as "same," "better" or "worse" (table 2, items J, K and L) is an attempted correlation of the entire 1939 pollinosis syndrome as described by the patient and observed by us in comparison with the symptoms of the 1938 season. It is our impression that the clinical differences in the two groups were much wider than the statistical percentages indicate. Thus the level of improvement in the "better" patients of the parenteral group is higher than the approximate 2 to 1 ratio conveys; and, on the other hand, "worse" includes severe aggravation of symptoms in several patients of the oral group but in none of the parenteral group.

An observation of particular note is the increased incidence of asthma (table 2, item H) during the 1939 season in the oral group as compared with the control group: an increase of 25 per cent in the former while the latter remained stationary. This is made further evident by the observation (table 2, item I) that 50 per cent of the "hay fever only" patients in the oral group had asthma for the first time in 1939 as compared with 20 per cent in the parenteral group.

TABLE 3.—*Correlation of Results with the Maximum Pollen Dose in Thousands of Noon Units*

Maximum Daily Pollen Dose, Units	Not Improved	Improved	Total Number Patients	Degree of Improvement: Slight	Moderate	Good	Excellent
30 thousand..	2	0	2	0	0	0	0
60 thousand..	13	4 23.5%	17	0	2 11.8%	2 11.8%	0
90 thousand..	3	1 25%	4	0	1 25%	0	0
120 thousand..	45	19 30%	64	6 9.4%	5 7.8%	7 10.9%	1 1.6%
180 thousand..	29	8 21.6%	37	1 2.7%	5 13.5%	2 5.4%	0
240 thousand..	3	2 40%	5	1 20%	0	0	1 20%
240+ thousand	4	8 66.7%	12	1 8.3%	6 50%	1 8.3%	0
Totals.....	99	42 29.8%	141	9 6.4%	19 13.5%	12 8.5%	2 1.4%

Percentages are in terms of the total number of patients in the same horizontal.

COMMENT

In this comparison of two therapeutic procedures we conclude that parenteral treatment with pollen extract was definitely more effective than oral ingestion of pollen, despite an enormous preponderance of dosage in the latter.

However, the 25 per cent of improved cases in the oral group cannot be dismissed as of no significance on the evidence of this series alone. If we are to charge these apparent improvements to chance variations in exposure or susceptibility or to the influence of mental suggestion, a like restriction must be put on all reports of pollen therapy.

SUMMARY

1. The results of treatment of thirty-two patients with ragweed pollinosis by the oral ingestion of pollen were definitely inferior to those of a control group of twenty-five patients treated by the subcutaneous injection of pollen extract.

2. Of those treated orally 25 per cent reported improvement compared with 56 per cent of those treated parenterally.

3. Severe gastrointestinal symptoms occurred in 12.5 per cent of the oral pollen cases and minor gastrointestinal discomfort in another 12.5 per cent.

4. No asthmatic or anaphylactoid symptoms occurred.

RESULTS OF ORAL POLLEN THERAPY[19]

BY DRS. SAMUEL M. FEINBERG AND JOHN SHELDON

In these clinics twenty-seven patients received oral pollen therapy, all except one also receiving placebo injections. None were given oral placebos. There were eleven males and sixteen females. The ages ranged from 8 to 74 years, and only two children were included. Of the group twelve had asthma with their hay fever. Ten had hypodermic treatment for one to two years prior to 1938, with satisfactory results in nine. The others had never had pollen injections. The method of administration was as outlined in the introduction, the maximum daily dose being 30,000 Noon or pollen units in two cases, 90,000 units in two, 120,000 units in one, 180,000 units in fifteen, 240,000 units in two, 270,000 units in three, 360,000 units in one and 540,000 units in one. The total ingestion for the entire period was from about 0.2 to 10 million units in the majority of instances, one patient receiving as much as 25,000,000 units (25 Gm.).

In twelve cases there were gastrointestinal reactions, ranging from slight discomfort and gaseous distention to nausea, abdominal pain and diarrhea. The doses causing the reactions were usually small, and with increasing doses the symptoms disappeared in the majority. This may be regarded, perhaps, as preliminary evidence of a decrease in the local allergy. In two patients there were one or two mild attacks of hay fever and asthma. It is not at all certain, however, that these were constitutional reactions since these individuals were susceptible to minor attacks of respiratory allergy out of season.

In twenty-three of our patients no indication of benefit was observed. In one patient the hay fever was slightly benefited while in another it was moderately benefited. Of two patients with hay fever and asthma the former appeared to be definitely improved although the asthma remained as in previous seasons. It appears, then, that in this group of patients several showed some relief from the nasal symptoms but none obtained relief from the asthma. Since asthma is almost always a later manifestation in the progress of pollinosis and since in hypodermic therapy the relief obtained from the asthma is more certain and is apt to occur before the relief of hay fever, it would appear that more reliance can be based on asthmatic symptoms in evaluating the results. Our present observations corroborate our past experiences and strengthen the impression that the value of oral pollen therapy is questionable.

GENERAL DISCUSSION

Under the circumstances of this study, in which there have been several groups of investigators working independently in different clinics, a considerable variation in results was to be anticipated.

Such variation is found in the extremes represented by the reported improvement of 100 per cent of the small pediatric series observed by one of us (E. P.) in contrast to the 14.8 per cent of the Northwestern-Michigan series. On the other hand, the statistics of

19. From the Allergy Division, Department of Medicine, Northwestern University Medical School, and the Allergy Division, Department of Medicine, University of Michigan Medical School.

the three larger groups show a much closer approximation, the improvement reported in the main Illinois series occurring in 26.8 per cent of seventy-one patients; in the Rush series, 25 per cent of thirty-two patients, and in the Northwestern-Michigan series, 14.8 per cent of twenty-seven patients. The pooled results of all the clinics presented in tables 3 and 4 yield the fact that in 29.8 per cent of 141 cases there was an apparent improvement under oral pollen therapy.

That this percentage is more impressive in the statistics than it was in the clinics is made apparent by the further breakdown of the figures into degrees of improvement. From these it appears that only two (1.4 per cent) of the 141 patients obtained "excellent" results; that twelve (8.5 per cent) obtained "good" results, and that the remaining twenty-eight (19.9 per cent) were in the columns indicating "slight" to "moderate" improvement.

Moreover it was in the relief of asthma, the touchstone of pollen therapy, that the oral treatment showed to least advantage. In the main Illinois series only 18 per cent of the asthma patients showed improvement compared with 37.5 per cent of the patients with uncomplicated hay fever—a reversal of the common experience with the injection method of treatment. In the Northwestern-Michigan series, of the twelve asthma patients none showed relief of the asthma, although two had some abatement of the nasal symptoms. In the Rush series there was a 25 per cent increase in the incidence of asthma in comparison with the season in which no treatment was given, owing to the fact that 50 per cent of the patients with the previously uncomplicated hay fever contracted asthma for the first time in 1939.

Controls.—Extended comment on the parenteral control series is unnecessary. Its purpose was to provide a treated control group, comparable in season, duration of treatment, type and selection of patient. Its results are somewhat less favorable than general experience with this mode of therapy but sharply superior to those of the companion oral group.

The placebo control group furnished surprising statistics. The 21.9 percentage of improvement in the thirty-two cases in which placebo capsules were received (table 1) approximates the 29.8 per cent of improvement noted in the combined group given oral pollen (tables 3 and 4). This becomes more striking in that two (6.25 per cent) of the patients receiving the starch capsules reported "excellent" relief compared with only 1.4 per cent of those treated with pollen capsules.

The implications of these data are apparent and challenging. At the very least, the placebo report detracts substantially from the significance of the percentages of improvement with oral pollen, if it does not wholly nullify it. We recognize also that the figures impinge proportionately on the control parenteral group and indeed on all reports of pollen therapy. We have here one more example of the need of caution in interpreting results based, however necessarily, on clinical impressions in the absence of sharply defined objective criteria.

Reactions.—Reactions of an untoward nature were mainly gastrointestinal. These occurred in 33 per cent of the combined series and, while severe in some instances, were for the greater part readily controllable by fractionating the dose.

Preseasonal attacks of hay fever were noted during the course of oral treatment in eleven (7.8 per cent) patients and asthma, either alone or in association with other symptoms, in five patients (3.6 per cent) of the combined series. Whether or not there were instances of systemic reactions was not wholly determinable. The failure by one of us (B. Z. R.) to elicit such reactions by the ingestion of large initial doses of pollen would be evidence against absorption to the point of systemic reaction.

Dosage.—Tables 3 and 4 present the range of dosage in relation to the spread of improvement. No definite conclusions seem warrantable.

In table 4 it is obvious that the results did not follow in direct proportion to the mass of dosage. The 6 to 10 million unit group of twenty-eight patients and the 10 to 15 million unit group of twenty-six are comparable numerically, but the percentage of improvement in the former is double that in the latter. If any inference can be made it is that the optimum mass dose lies between 4 and 10 million Noon units of ingested pollen.

TABLE 4.—*Correlation of Results with Total Amount of Pollen Ingested in Millions of Noon Units*

Total Pollen Ingested, Units	Not Improved	Improved	Total Number Patients	Degree of Improvement			
				Slight	Moderate	Good	Excellent
0.5-1 million...	4	0	4	0	0	0	0
1-2 million.....	9	0	9	0	0	0	0
2-4 million.....	36	15 29.4%	51	4 7.8%	6 12%	4 7.8%	1 2%
4-6 million.....	12	8 40%	20	2 10%	2 10%	4 20%	0
6-10 million....	15	13 46.8%	28	3 10.7%	6 21.4%	4 14.3%	0
10-15 million....	20	6 23%	26	0	5 19.2%	0	1 3.8%
15-30 million....	3	0	3	0	0	0	0
Totals.....	99	42 29.8%	141	9 6.4%	19 13.5%	12 8.5%	2 1.4%

Percentages are in terms of the total number of patients in the same horizontal.

The table of maximum daily doses (table 3) is heavily weighted by the exceptional results of the small pediatric series. Seven of the twelve patients receiving in excess of 240,000 units were members of that group. Here again results bear no consistent relation to dosage. It is true that the highest percentages are seen with the highest maximum dosage, but their statistical significance is greatly impaired by the relative paucity of cases in these groups. In the two largest groups of cases, the 120,000 unit maximum dose shows to slight advantage over the 180,000 unit dose.

CONCLUSIONS

1. In our appraisal of oral pollen therapy on the basis of our combined results the opinions of the investigators diverge from a complete rejection to a limited acceptance.

2. We concur in the opinion that the oral ingestion of pollen, in the doses used in this inquiry, is a safe procedure; that gastrointestinal reactions are frequent and troublesome, sometimes severe, but not dangerous, and that its therapeutic effectiveness is, at the highest estimate, of a minor grade, particularly in the control of asthma, and definitely inferior to that obtainable by the parenteral injection of pollen extract.

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EFFECT OF HISTAMINASE

ON HISTAMINE INTOXICATION, TUBERCULO-ANAPHYLAXIS AND TUBERCULO-ALLERGY

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The problem of tuberculosis has been involved so intimately with the conceptions of tuberculo-anaphylaxis, tuberculo-allergy and specific immunity that within recent years it was brought to fundamentally close approximation to the conceptions evolved on the theoretical bases of histamine action in the body. These actions in general were reviewed elaborately by Best and McHenry in 1931,[1] when they pointed out that there appears to be a striking relation between histamine shock and anaphylactic shock as based on the observations of Dale and Laidlaw (1910-1920) and others. In 1929 Best [2] showed that lung and other tissues when suspended in saline solution and incubated in the presence of toluene at 37 C. cause the disappearance of naturally occurring or added histamine. The substance or system producing this disappearance is thermolabile. In 1930 Best and McHenry [3] suggested the name histaminase for a histamine-inactivating substance with the characteristic of enzymes. They found the richest sources in the dog to be the kidney and intestine, less being present in the lungs. The histamine-histaminase reaction is inhibited by lack of oxygen and by small amounts of cyanide. Perfusion experiments showed that isolated kidneys inactivate histamine much more rapidly than liver, heart and hind limbs of the dog. They stated at that time:

> Since it has not been established that histamine is the causative agent in any pathological condition there would be no obvious clinical application of histaminase, even if it should be established that the ability of an organism to inactivate histamine can be increased by administration of the enzyme.

Since that time, numerous attempts have been made to establish the identity of histamine action and disease, to apply histaminase in vivo for treatment of certain diseases and to inactivate histamine itself. A successful attempt to neutralize the toxic action of histamine by histaminase and also to prevent anaphylactic shock by the prior administration of histaminase in the guinea pig was recorded in 1939 by Karady and Browne.[4] They found that the intravenous injection of 3 units (3 ampules) of histaminase-Winthrop (Torantil T 360) in guinea pigs—1 unit of histaminase is the amount necessary to detoxify in vitro 1 mg. of "histamine dihydrochloride"—fifteen minutes before the intra-abdominal injection of 4 mg. of histamine prevented the symptoms of histamine shock in most instances. Of ten control animals, all showed marked symptoms within five to seven minutes, and seven animals died shortly. Of the twenty animals pretreated with histaminase, six showed slight symptoms after fifteen minutes, but they disappeared in a few minutes in all but two animals, which died thirty-five minutes after the injection of the histamine. Histaminase (3 units) given intravenously fifteen minutes before the intra-abdominal administration of egg white (2 cc. of 50 per cent solution) to previously sensitized guinea pigs prevented an anaphylactic shock completely in fifteen of twenty animals. The other five guinea pigs showed only very slight symptoms beginning twenty minutes after the injection of egg white and lasting for a few minutes. Of the ten control animals, all showed severe anaphylactic shock developing within five to ten minutes, and four animals died from ten to fourteen minutes after the injection of the egg white.

In the light of our recent analysis of the tubercle bacillus and its natural products by immune, allergic and anaphylactic tests,[5] these results with histamine and histaminase, and anaphylaxis and histaminase, appeared to offer exceptional opportunities for the solution of a little understood problem in tuberculosis and in allergy in particular. These observations showed that the bacillary body of the tubercle bacillus sensitizes primarily to tuberculo-allergy and serves to immunize against virulent infection, while the natural filtrate containing tuberculoprotein sensitizes to anaphylaxis, provokes anaphylactic shock and allergic intoxication but does not sensitize to allergy or immunize specifically against virulent infection. From these observations, it was concluded that tuberculo-anaphylaxis, tuberculo-allergy and tuberculo-immunity show distinctive characteristics indicating that they are separate and apparently unrelated biologic phenomena.

TABLE 1.—*The Effect of Histaminase on Tuberculo-Anaphylaxis in Guinea Pigs*

Sensitizing Injection, Amount of Tuberculoprotein in Seitz Filtrate *	Histaminase, Amount Given Intravenously (Via Ear Vein)	Amount of Natural Seitz Filtrate Given Intravenously and Interval After Sensitizing Injection	Interval Following Histaminase Injection When Intoxicating Injection Was Given	Results
5.0 mg.	4 units	2 cc. (1.1 mg. tuberculoprotein) 59 days	15 minutes	Died 3 minutes
5.0 mg.	6 units	2 cc. (1.1 mg. tuberculoprotein) 59 days	30 minutes	Died 3 minutes
5.0 mg.	6 units	3 cc. (1.7 mg. tuberculoprotein) 59 days	4 hours	Died 3 minutes
5.0 mg.	6 units	2 cc. (1.1 mg. tuberculoprotein) 59 days	24 hours	3+ reaction; recovered †
5.1 mg.	6 units	2 cc. (1.9 mg. tuberculoprotein) 55 days	24 hours	Died 2 minutes
5.1 mg.	6 units	2 cc. (1.9 mg. tuberculoprotein) 55 days	24 hours	Died 2 minutes
3.2 mg.	6 units	2 cc. (1.9 mg. tuberculoprotein) 46 days	24 hours	Died 2 minutes
5.1 mg.	28 units	1.5 cc. (1.4 mg. tuberculoprotein) 72 days	30 minutes	Died 2 minutes
12.8 mg.	26 units	2 cc. (1.9 mg. tuberculoprotein) 63 days	24 hours	Died 2 minutes
12.8 mg.	26 units	2 cc. (1.9 mg. tuberculoprotein) 63 days	48 hours	Died 2 minutes

* Determined by trichloroacetic acid precipitation (Seibert). References: Corper, H. J., and Cohn, Maurice L.: The Effects of Tuberculoprotein: A Quantitative Study, J. A. M. A. **112**: 403-408 (Feb. 4) 1939; Intoxication in Tuberculosis, Am. Rev. Tubere. **41**: 71-86 (Jan.) 1940.

† Almost lethal.

From the Research Department, National Jewish Hospital.

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By means of the appropriate use of histaminase, and in the light of Karady and Browne's observations, it was hoped that we might be able to discern whether the intoxication in tuberculo-anaphylaxis or in tuberculo-allergy, or both, was histamine shock or intoxication, whether one or both could be combated by the appropriate use of histaminase, and, if they did not react alike, possibly to obtain additional evidence of the difference in these reactions. Accordingly, the effect of histaminase on tuberculo-anaphylaxis and tuberculo-allergy in the guinea pig was studied.

THE EFFECT OF HISTAMINASE ON TUBERCULO-ANAPHYLAXIS AND TUBERCULO-ALLERGY

Accepting the previous in vivo observations concerning the effect of histaminase on histamine intoxication and anaphylactic shock in the guinea pig on face value, it appeared necessary in the early part of our studies to be certain of the potency of the histaminase preparations we used.[6] Accordingly, we followed the O. W. Barlow method for in vitro estimation of histaminase, which had to be modified slightly for our special purposes of using a lethal test instead of the usual test involving lowering of blood pressure.

METHOD OF ASSAY OF HISTAMINASE

Buffer solution (p_H 7.35 to 7.4) was prepared by dissolving 7.6 Gm. of disodium phosphate ($Na_2HPO_4 \cdot 12H_2O$) and 0.7 Gm. of sodium biphosphate ($NaH_2PO_4 \cdot H_2O$) in 262 cc. of recently boiled distilled water. The test was set up as follows: Tube 1 contained 15 cc. of buffer solution, 3 cc. of distilled water and 1 mg. of histamine hydrochloride; tube 2, 15 cc. of buffer solution, 2 cc. of distilled water, 1 cc. (1 unit) of histaminase and 1 mg. of histamine hydrochloride; tube 3, 15 cc. of buffer solution, 2 cc. (2 units) of histaminase and 1 mg. of histamine hydrochloride. The tubes were saturated with oxygen, placed in a shaking machine for twenty-four hours at 37.5 C. and then used for intravenous (ear vein) injection in guinea pigs (no anesthetic or drugs were used which might confuse the results).

RESULTS WITH FIRST SUPPLY OF HISTAMINASE

Tube 1, Control.—Histamine hydrochloride, 3 cc. (0.17 mg.), injected into an 820 Gm. guinea pig made the animal extremely ill but the animal recovered; 5 cc. (0.28 mg.) injected into a 1,040 Gm. guinea pig was lethal in three minutes.

Tube 2.—One unit of histaminase and 1 mg. of histamine hydrochloride, 4.5 cc. (0.25 mg.), injected into a 395 Gm. guinea pig was lethal in one minute, and 9 cc. (0.5 mg.) injected into a 1,204 Gm. guinea pig was lethal in two minutes.

Tube 3.—Two units of histaminase and 1 mg. of histamine hydrochloride were used. The entire tube of 18 cc. was injected into a guinea pig without effect.

Conclusion.—Two units of histaminase completely destroyed 1 mg. of histamine hydrochloride, while 1 unit did not completely destroy 1 mg. of histamine hydrochloride.

RESULTS WITH SECOND SUPPLY OF HISTAMINASE

Histamine hydrochloride, 3 cc. (0.17 mg.), was lethal to a 1,000 Gm. guinea pig in two minutes. One unit of histaminase plus 1 mg. of histamine hydrochloride, 18 cc., was lethal to a 1,110 Gm. guinea pig in two minutes, while 9 cc. was not lethal but gave a pronounced histamine reaction. One unit of histaminase plus 0.5 mg. of histamine hydrochloride and 2 units of histaminase plus 1 mg. of histamine hydrochloride showed complete destruction of the histamine.

Conclusion.—Two units of histaminase completely destroyed 1 mg. of histamine hydrochloride in vitro as determined by intravenous toxicity in the guinea pig.

TABLE 2.—*The Effect of Histaminase on General Tuberculo-Allergic Intoxication*

Sensitizing Injection Given Subcutaneously (Tubercle Bacilli)	Amount of Histaminase Given Intravenously (Ear Vein)	Interval After Sensitization and Route of Intoxicating Injection of 5 Cc. Natural Seitz Filtrate (4.7 Mg. Tuberculoprotein)	Interval After Histaminase Injection When Intoxicating Injection Was Given	Results
1 mg. avirulent human tubercle bacilli	4 units	Intraperitoneally, 101 days	15 minutes	Died 36 hours
	4 units	Intraperitoneally, 101 days	15 minutes	Died 18 hours
		Intraperitoneally, 101 days	.....	Died 36 hours
		Intraperitoneally, 101 days	.....	Marked toxicity; recovered
	4 units	Intraperitoneally, 40 days	15 minutes	Marked toxicity, recovered
	4 units	Intraperitoneally, 40 days	15 minutes	Died 36 hours
		Intraperitoneally, 40 days	.....	Died 36 hours
		Intraperitoneally, 40 days	.....	Died 22 hours
	4 units	Intraperitoneally, 40 days	24 hours	Died 15 hours
	4 units	Intraperitoneally, 40 days	24 hours	Marked toxicity, recovered
	4 units	Intraperitoneally, 40 days	24 hours	Marked toxicity, recovered
		Intraperitoneally, 40 days	.....	Died 36 hours
		Intraperitoneally, 40 days	.....	Marked toxicity, recovered
		Intraperitoneally, 40 days	.....	Died 36 hours
0.0001 mg. virulent human tubercle bacilli	4 units	Intraperitoneally, 40 days	15 minutes	Died 15 hours; tuberculosis 2+*
	4 units	Intraperitoneally, 40 days	15 minutes	Died 24 hours; tuberculosis 2+
		Intraperitoneally, 40 days	.....	Died 15 hours; tuberculosis 2+
		Intraperitoneally, 40 days	.....	Died 18 hours; tuberculosis 2+
1 mg. avirulent human tubercle bacilli	10 units	Subcutaneously, 46 days	24 hours	Marked toxicity; recovered
	10 units	Subcutaneously, 46 days	24 hours	Died 18 hours
	10 units	Subcutaneously, 46 days	24 hours	Died 30 hours
		Subcutaneously, 46 days	.....	Marked intoxication; recovered
		Subcutaneously, 46 days	.....	Died 72 hours
		Subcutaneously, 46 days	.....	Died 18 hours
	20 units	Subcutaneously, 84 days	24 hours	Died 21 hours
		Subcutaneously, 84 days	.....	Died 16 hours
0.0001 mg. virulent human bacilli	20 units	Subcutaneously, 67 days	24 hours	Died 8 hours tuberculosis 3+
		Subcutaneously, 67 days	.....	Died 8 hours tuberculosis 3+

* The amount of tuberculous involvement found in these guinea pigs is graded from 0 to 4+, from no visible macroscopic tuberculosis to a profound generalized tuberculosis.

6. The histaminase was supplied for these studies in 2 unit ampules by the Winthrop Chemical Company, Inc., which assisted during these investigations. Their original assay, 2 units per ampule of histaminase, was reassayed by them, giving 1.4 units and 1.24 units for the first and second batches respectively. This product does not stand accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

TUBERCULO-ANAPHYLAXIS

Tuberculo-anaphylaxis results in guinea pigs from the sensitization with suitable amounts of tuberculoprotein, contained in the filtrate from growing tubercle bacilli on the Wong-Weinzirl nonprotein medium, and from giving an intravenous intoxicating injection of the same filtrate containing tuberculoprotein after from two weeks to at least six months or more. The route of intoxicating injection must be intravenous in distinction to the allergic intoxication, to be considered later, in which any parenteral route can be used.

In table 1 are recorded the results of an attempt to protect guinea pigs against lethal tuberculoprotein anaphylactic shock.

In spite of the fact that the guinea pigs recorded in table 1 were given from 4 to 28 units of histaminase intravenously and that intervals varying from fifteen minutes to forty-eight hours were allowed to elapse before the intoxicating intravenous injection of tuberculoprotein (filtrate) was administered, no appreciable

TABLE 3.—*The Effect of Histaminase on Tuberculin Cutaneous Reaction (Tuberculoprotein Cutaneous Hypersensitiveness)*

Subcutaneous Sensitization Injection of Tubercle Bacilli	Tuberculin Cutaneous Reaction 24 Hours After Intracutaneous Injection of 1: 100 Seitz (Tuberculoprotein) and Interval After Sensitization Injection		Amount of Histaminase Given 15 Minutes Prior to Cutaneous Filtrate (Tuberculoprotein) Injection	Tuberculin Cutaneous Reaction 24 Hours After Intracutaneous Injection of Seitz Filtrate (Tuberculoprotein)
1 mg. avirulent human	3+*	82 days	4 units	2+
	3+	82 days	4 units	2+
	2+	82 days	4 units	2+
	3+	82 days	4 units	2+
	2+	82 days	.....	2+
	3+	82 days	.....	2+
	3+	82 days	.....	3+
	2+	82 days	.....	2+
		83 days	20 units	2+
		83 days	.....	2+
0.0001 mg. virulent human	...	67 days	20 units	3+
	...	67 days	.....	2+

* The cutaneous tuberculin reactions are graded arbitrarily from 0 to 4+; from no visible reaction beyond that produced by a saline control to a marked erythematous, edematous reaction about 2 cm. in diameter with a central area of necrosis.

effect on the lethal anaphylactic shock was noted. The lethal effect was not retarded in any way in comparison with the effect on guinea pigs not treated with histaminase (not tabulated here because of its similarity to the former and to conserve space).

TUBERCULO-ALLERGY

General Allergic Intoxication.—Tuberculo-allergy was produced in guinea pigs by the injection of human tubercle bacilli (avirulent or virulent). If intoxication is desired after an appropriate interval, the parenteral (intravenous, subcutaneous or intraperitoneal) injection of tuberculoprotein (filtrate) in suitable amount is administered. A profound, slowly evolving intoxication results from the second intoxicating injection, not resembling anaphylactic intoxication, with death, when it occurs, ensuing in from a few hours to seventy-two hours.

An attempt to neutralize the general allergic intoxication in guinea pigs by histaminase injected intravenously is recorded in table 2.

An examination of the data recorded in table 2 indicates that no appreciable retardation of general tuberculo-allergic intoxication is produced by histaminase in amounts ranging from 4 to 20 units given to guinea pigs intravenously fifteen minutes and twenty-four hours prior to an intraperitoneal or subcutaneous intoxicating injection of tuberculofiltrate (tuberculoprotein), regardless of whether the tuberculo-allergy was induced by avirulent or virulent (progressive tuberculosis-inducing) human tubercle bacilli.

Tuberculocutaneous Hypersensitiveness (Cutaneous Tuberculin Reaction).—Even though no effect of histaminase was noted on the general tuberculo-allergic

TABLE 4.—*The Effect of Histaminase on Histamine Intoxication*

Weight of Guinea Pigs in Grams	Amount of Histaminase Given Intravenously	Amount and Route of Histamine Hydrochloride Injection	Time Interval After Histaminase when Histamine Hydrochloride Was Injected	Results
1,015	4 units	0.5 mg. intravenously	18 minutes	Died 4 minutes
955	.....	0.5 mg. intravenously	.....	Died 2 minutes
945	4 units	4.0 mg. intraperitoneally	15 minutes	Died 45 minutes
900	.....	4.0 mg. intraperitoneally	.....	Markedly toxic; recovered
1,155	10 units	0.3 mg. intravenously	15 minutes	Died 2 minutes
840	10 units	0.25 mg. intravenously	15 minutes	Died 3 minutes
1,385	.....	0.25 mg. intravenously	.....	Died 1 minute
1,000	.....	0.3 mg. intravenously	.....	Died 2 minutes
1,020	20 units	0.3 mg. intravenously	15 minutes	Died 1 minute
748	10 units	0.25 mg. intravenously	30 minutes	Died 3 minutes
1,103	20 units	4.0 mg. intraperitoneally	15 minutes	Died 33 minutes
905	20 units	4.0 mg. intraperitoneally	15 minutes	Died 90 minutes
1,010	20 units	4.0 mg. intraperitoneally	15 minutes	Died 30 minutes
1,140	.....	4.0 mg. intraperitoneally	.....	Markedly toxic; recovered
1,240	.....	4.0 mg. intraperitoneally	.....	Markedly toxic; recovered
1,050	.....	4.0 mg. intraperitoneally	.....	Markedly toxic; recovered
226	4 units	4.0 mg. intraperitoneally	15 minutes	Died 8 minutes
255	4 units	4.0 mg. intraperitoneally	15 minutes	Died 9 minutes
203	.....	4.0 mg. intraperitoneally	.....	Died 13 minutes
225	.....	4.0 mg. intraperitoneally	.....	Died 14 minutes
846	10 units	6.0 mg. intraperitoneally	30 minutes	Died 18 minutes
872	10 units	6.0 mg. intraperitoneally	90 minutes	Died 20 minutes
818	10 units	6.0 mg. intraperitoneally	24 hours	Died 24 minutes

intoxication, it was thought possible that some effect of the histaminase might be exerted on the cutaneous hypersensitiveness to tuberculoprotein. In order to determine this possible effect, guinea pigs were sensitized allergically by appropriate bacillary injections and then were tested at a suitable time for tuberculoprotein (filtrate) cutaneous reactivity before and after histaminase treatment. The results of these tests are recorded in table 3.

The data concerning the effect of intravenous histaminase injections on cutaneous hypersensitiveness in tuberculo-allergic guinea pigs recorded in table 3 indicate that the histaminase given intravenously in amounts of 4 and 20 units fifteen minutes before the intra-

cutaneous injection of a tuberculin testing dose (1:100 dilution of natural filtrate) revealed no appreciable inhibitory effect on the development of the specific cutaneous reaction resulting in twenty-four hours, as recorded in table 3, or at any time during the usual forty-eight hours' observation period. The slight retardation in the reactions noted in the second as compared with the first intracutaneous test with tuberculoprotein, which was found both in the controls and in the histaminase-treated animals, possibly may be accounted for by a slight desensitizing effect of the first tuberculoprotein injection itself.

EFFECT OF HISTAMINASE ON IN VIVO HISTAMINE INTOXICATION

In view of the foregoing negative effects of histaminase on the intoxication of tuberculo-anaphylaxis and tuberculo-allergy, it appeared advisable to check our results. If for no other reason than for academic purposes, it would be useful in trying to explain the possible absence of the relation of histamine to these intoxications. Therefore we repeated the in vivo histaminase-histamine neutralization experiments reported by others. In our experiments attempting to neutralize a lethal toxic unit of histamine, we used both intravenous and intraperitoneal intoxicating routes. The detailed results of these experiments in guinea pigs are recorded in table 4.

The tests, recorded in table 4, attempting to neutralize histamine intoxication by prior (from fifteen minutes to twenty-four hours) intravenous histaminase injections showed no appreciable detoxicating effect of the histaminase injections on approximately 1 unit, a lethal amount, of histamine hydrochloride, regardless of whether the latter was administered intravenously or intraperitoneally to the guinea pigs, and even though the histaminase in in vitro tests using 2 units was able completely to detoxicate 1 mg. of histamine hydrochloride in twenty-four hours, as tested by intravenous injection of the final material into guinea pigs. The intoxicating dose of histamine hydrochloride given by intravenous injection was about one tenth the amount given by the intraperitoneal route.

SUMMARY AND CONCLUSIONS

In an attempt to clarify the mechanism of tuberculo-anaphylactic and tuberculo-allergic intoxication, histaminase of tested in vitro strength was given intravenously to guinea pigs, which had been appropriately sensitized prior to an intoxicating injection of the specific tuberculoprotein without, however, appreciably neutralizing or retarding the tuberculo-anaphylactic or tuberculo-allergic intoxication (general or cutaneous hypersensitiveness). In controlling these observations, it was found impossible to neutralize a single lethal general intoxicating amount of histamine hydrochloride when the histaminase was given from fifteen minutes to twenty-four hours prior to the intravenous or intraperitoneal histamine injection or when the amount of histaminase used was as much as 20 units.

From these observations, it still remains impossible to suggest whether tuberculo-anaphylactic or tuberculo-allergic intoxications or reactions are based on histamine reactions or liberation, for which purpose these experimental investigations were primarily performed. For these reasons, it would not appear that histaminase has a place at present in the therapy of tuberculo-allergic conditions.

TYPHOID FEVER OCCURRING IN IMMUNIZED PERSONS

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CHICAGO

The success of typhoid immunization in preventing the outbreak of widespread epidemics of the disease has been so complete that there has been relatively little opportunity for studying the disease in persons so immunized.[1] When the epidemic on which this report is based developed in a population 90 per cent of which had been immunized against typhoid fever, the value of a clinical and statistical study was suggested to me.[2] The prevailing war conditions made necessary frequent and unforeseen changes in the personnel and eventually mass evacuations from the hospital; in the resulting confusion the detailed clinical, laboratory and statistical records were lost. Nevertheless, the experiences obtained were so informative and some of the observations so striking that I felt that even a brief communication based on my personal notes and facts vividly impressed on my memory might have some value as an addition to the literature already existing on this subject.

The military hospital at Vich, Spain, an old convent, was made ready for occupancy five days before the arrival of hospital personnel. On his arrival the medical director of the hospital consulted with the city authorities and the city bacteriologist. It was found that this old convent was supplied with water from three different sources and that the water was conducted to the convent in leaden pipes, which had been so inextricably connected up to each other that it was a several days job to separate the various sources of water supply. There were three sources which emptied into a large common iron reservoir that was placed in the top story under the roof of the convent. From the city bacteriologist it was learned that one of these sources of supply was fairly uncontaminated and constantly had a low bacterial count. The second source of supply was supposed to be fairly uncontaminated at high water, but during the dry season it was regularly contaminated with all kinds of impurities. The third source of supply, the convent pump, drew surface water from a well situated in the convent gardens, and this well, as all similar wells in the city of Vich, had been for centuries badly contaminated with typhoid organisms and all kinds of impurities. The two contaminated sources were disconnected and joined to one tank, the water of which was colored red with permanganate and led off into taps, each of which not only delivered this red water but was furthermore marked with a sign, "nonpotable water." It was necessary to have this additional supply as the needs of the institution greatly exceeded the available drinking water. The tank which contained water from the uncontaminated source of supply was thoroughly chlorinated and kept so, and this water was led off into taps that were marked "potable water." To

1. Vaughan, V. C., Jr.: Typhoid Fever in the American Expeditionary Forces, J. A. M. A. **74**: 1074 (April 17) 1920. Burrage, T. J.: Mil. Surgeon **70**: 231 (March) 1932. Labbé, M.: Ann. de méd. **3**: 13 (Jan.) 1916. Stintzing, R.: München. med. Wchnschr. **75**: 25 (Jan. 6) 1928. Lovaglio, R.: Gazz. med. di Roma **52**: 149 (Aug.) 1926. Gadrat, J.: Progrès méd., Sept. 5, 1931, p. 1556. Monnier, M.: Rev. méd. de la Suisse Rom. **58**: 301 (April 25) 1938. Coburn, H. C., Jr.; Ostrander, F. R., and Gillespie, J. O.: Mil. Surgeon **76**: 133 (March) 1935.

2. Dr. Leo Eloesser, of San Francisco, suggested the study, outlining methods of procedure, and continued his interest in this study. He also supplied the information on the source of infection.

effect this change, however, took several days, and the infection probably occurred a good many days before this change could be made.

The epidemic broke out in the military hospital at Vich in the last week of April 1938, about one month after the hospital had been established. At this time the hospital had approximately 1,700 patients and a staff of about 200. The source of the infection was one of three water supplies of the hospital which had become contaminated from the overflow of an adjacent sewage system. Admissions and discharges to and from the hospital were prohibited from the time of the discovery of the disease until two weeks after it had been brought under full control. Thus the population of the hospital was constant for a period of five weeks. Questioning of this effective revealed that about 10 per cent had never been vaccinated against typhoid fever while the remaining 90 per cent had received two or more injections of typhoid vaccine from one year to three months prior to the epidemic.

Altogether there were 147 cases of typhoid proved by Widal tests and positive cultures from the blood, urine or stools and in several cases from all three sources. However, in the month preceding and during this time practically everybody in the hospital suffered some form of gastrointestinal disturbance. This consisted of malaise, headache, backache, a feeling of fulness in the abdomen associated with diarrhea (less often constipation) and sometimes slight grades of fever. Owing to limited facilities laboratory studies could not be done but it is highly probable that many of these too were mild typhoid infections.

Of those with proved typhoid forty-nine had never been immunized against the disease, or approximately 25 per cent of the 190 unprotected patients and staff members in the hospital. The remaining ninety-eight patients had been previously immunized, thus giving an incidence of 6 per cent for the immunized effective of the hospital. The total incidence of the entire hospital was about 7.5 per cent.

CLINICAL COURSE

Only fourteen patients (14.3 per cent) in the immunized group showed the classic features and course of the disease as it appeared in the nonimmunized patients. Of the remaining, a third (about 28 per cent of the total immunized group) ran a mild and abbreviated but otherwise typical course of typhoid fever. The third and largest group (53 per cent of the immunized patients) was atypical in many respects and demonstrated few constant features but these were also most constant for the series as a whole. Dissociated pulse and temperature, i. e. relative bradycardia, was by far the most notable, being almost invariably present in all the cases, typical and atypical, of typhoid fever. In almost all cases the pulse was 80, 90 and rarely over 95, associated with temperatures as high as 104.5 F. Late in the course of the disease and associated with symptoms of toxic myocardial changes the pulse increased and was of grave prognostic import.

Splenomegaly was second only to the relative bradycardia as a constant feature. In the series of ninety-eight immunized patients, sixty showed some enlargement of the spleen. In the present series actual leukopenia was not a frequent occurrence, but white blood counts within normal limits were the rule even when there were marked elevations of temperature. Less impressive from the diagnostic point of view but next in the order of constancy was the "characteristic" facies as described in the textbooks. The appearance of the tongue with its thickly furred dorsum and flaming red borders and triangle at the tip was even more characteristic.

The exanthem varied remarkably. With some patients the eruption appeared in four or five days, with others only after two, three and even four weeks, and fully half the immunized patients never had an eruption at all. The extent of the eruption also showed all possible variations. In some cases it was represented by only four or five pastel rose-colored flecks 1 mm. in diameter on the back or abdomen and in others all possible forms were seen. The most extreme case in this series closely resembled a case described by Labbé. My case occurred in a Canadian 25 years of age who had been immunized three months before contracting the disease. He had been running the typical course of a very severe typhoid fever infection for three weeks. Absence of the eruption was the only atypical feature. Suddenly toward the end of the third week and within twenty-four hours there developed several crops of spots in rapid succession that soon involved the entire body including the face, ears, neck and extremities. Only the palms, soles and genitalia were spared. The rash was a dusky dark purplish red slowly fading on pressure, macular and possibly very lightly raised. The macules measured 3 to 6 mm. in diameter and frequently coalesced to form irregular patches up to 1 and 1.5 cm. in diameter. The exanthem was so atypical that it seemed that a mistake in the diagnosis had been made and that my associates and I were dealing with a case of typhus or, failing that, of typhoid complicated by measles. However, the positive typhoid cultures, the increasing sensitivity of the Widal reaction, the leukopenia and the apathetic and quiet status of the patient ruled out the former while the absence of Koplik's spots, coryza and conjunctivitis spoke against a complicating measles. The further course of this patient was uneventful; three days later the temperature started the usual fall by lysis, and two weeks after the appearance of the rash the patient was afebrile and the eruption, having changed to a brownish discoloration, gradually and completely disappeared.

The temperature curves fell into three main categories: the typical prolonged curve of pyrexia with gradual stages of rise and defervesence, secondly a similar curve but with all three stages shortened, and finally in the largest group, a curve with no constant features and quite variable in form.

LABORATORY DATA

Although the presence of a Widal reaction in patients previously immunized had little diagnostic import per se, the variation in its sensitivity during the course of the disease was a very valuable guide to a correct diagnosis. On admission to the typhoid ward all our immunized patients had positive Widal tests. Seventy-two were positive in dilutions of 1 : 40, twenty at dilutions of 1 : 160, five at dilutions of 1 : 320 and only one at the maximum dilution used, 1 : 640. All patients showed a progressive increase in agglutinins during the course of the disease so that at the time of discharge all but three showed positive reactions in the highest dilutions. On the other hand there were three patients with fever of unknown etiology under observation, all of whom had been immunized against typhoid fever. One of these had a positive agglutination reaction in a

titer of 1:80 and the other two positive reactions in dilutions of 1:320. Successive Widal tests showed no further increase in agglutinins. Ultimately the diagnosis of brucellosis was made in two cases and amebiasis in the third.

Stool cultures were positive in the majority of cases at least once during the illness, and the frequency of positive cultures in the immunized group approximated the frequency in the nonimmunized group. Blood cultures for the nonimmunized group were positive only slightly less frequently than the stool cultures, but in the immunized group they were only about half as frequent. This discrepancy between the approximately equal frequency of positive stool cultures for the two groups and the difference in the frequency of positive blood cultures was interpreted as signifying that the bacteremia in the immunized group was of shorter duration and therefore the positive stage escaped detection by the infrequent cultures made. Because of the shortage of materials and the difficulties of transportation it was impossible to do more frequent blood cultures to throw more light on this interesting question.

COMPLICATIONS

Complications were uncommon in both groups but more frequent among the immunized patients. There were four patients who suffered relapses, three from the immunized group and only one from the nonimmunized group. This last patient, a nurse, had a total of three relapses before overcoming the disease and during the second relapse suffered a fairly severe intestinal hemorrhage, the only case of this complication in the entire series. Bronchopneumonia developed in two patients, one from each group; the nonimmunized patient died, the immunized patient recovered. The remaining three complications occurred in immunized individuals. One had a laryngeal ulcer that healed spontaneously after a week. The second had fatal typhoid meningitis. The third, who eventually succumbed to an overwhelming toxemia, developed a complication not described in the literature. This patient had a shrapnel wound in the form of an avulsion of muscle tissue in the lateral aspect of the middle third of the left thigh, which left a cone-shaped defect about 6 cm. in diameter and 3 cm. in depth at the apex. Two weeks after the onset of typhoid this region and the tissue bordering it for a distance of 3.5 cm. became dry, black and gangrenous, resembling very much noma of the face. Cultures from this gangrenous material were not made.

MORTALITY

Nine of the total of 147 cases terminated in death thus giving a mortality rate of 6.1 per cent for the entire series. Of these nine deaths five occurred in the nonimmunized group, a mortality of 10.2 per cent for this group, and four among the immunized patients, a mortality of 4 per cent.

TREATMENT

With the exception of the use of prostigmine for the relief of tympanites nothing new in the treatment of the disease can be reported. Because the value of the well known principles of treatment were so impressively demonstrated by the conditions under which we had to work, it seems worth while to emphasize these once more here.

Absolute bed rest is one of the most essential requirements in the care of these patients. Occasionally some of the patients would prevail on our inexperienced nurses to allow them to sit up in bed or squat alongside the bed to use the bedpan. Invariably this procedure was followed by a rise in temperature and complete exhaustion. Stimulants such as caffeine, epinephrine hydrochloride and camphor generally defeated their purpose because they greatly increased the restlessness of the patient, leading to exhaustion, rise in temperature and delirium, so that we came to prohibit these drugs unless they were absolutely indicated. Sedatives were used freely, the most effective being the barbiturates and chloral hydrate. To very restless and delirious patients who could not be controlled by these, one sixth grain (0.01 Gm.) of morphine, repeated in an hour if necessary, was given. It was gratifying to note the lowered temperature and improved appearance of the patient after a few hours of rest induced in this manner.

The problem of adequate nutrition was most difficult to solve. Butter, cream and eggs were not available. The milk was diluted and to be had only in small quantities. The bread was extremely coarse. The first two weeks of the epidemic the typhoid ward was a dismal place with bed after bed occupied by wasted patients completely apathetic and disinterested in themselves and in what was taking place about them. In desperation, caution was thrown to the winds. Protein requirements were made up by meats—canned chicken, tinned ham and bully beef—shredded and served in small portions. Caloric requirements were satisfied by puréed chick-peas, rice, toast and sugar up to the tolerance of the individual. In spite of this character of the diet, which would seem traumatic to normal intestinal tracts, striking improvement occurred in almost all patients, remarked on even by the nonmedical personnel. The patients gained in weight and concomitantly became much brighter and more interested, while the number of stuporous and delirious patients decreased notably.

The distressing and dangerous nature of tympanites in typhoid fever is usually understated. Probably because of the high sugar content of the diet and the toxicity of the particular epidemic there was a marked tendency toward distention in this series. Invariably associated with distention and roughly varying with its degree there also occurred a rise in temperature and pulse. With greater degrees of distention there occurred embarrassment of respiration, which in one case with most marked tympanites led to distinct cyanosis. Furthermore, although not occurring in any of the series presented, there is the increased danger of perforation as a result of the thinning out of the wall of the distended intestine and the ischemia resulting from the compression of intramural vessels supplying the necrotic Peyer's patches. Because the distention in this disease is of the paralytic or adynamic type, the first indication of this unpleasant complication is the decrease in peristaltic sounds. It became the practice in making rounds on the typhoid service not only to examine and palpate the abdomen but to listen to the peristaltic sounds as well.

Distention was treated by the usual measures including the reduction of the sugar content of the diet, enemas and return flow enemas. In spite of this, in three patients the distention increased to marked tympanites, one of the patients becoming cyanotic. It was then decided to try prostigmine to relieve the condition. Because of the theoretical possibility of precipitating a perforation it was used cautiously at first. It was found

that half an ampule (0.25 mg.) of prostigmine injected subcutaneously stimulated smooth mild peristalsis that caused a steady expulsion of flatus and rapid decrease in the distention. Thereafter one half ampule of prostigmine followed if necessary by the second half an hour later was given in all cases of distention that failed to respond promptly to change in diet and an enema. The drug was so given on thirty-one occasions to nineteen patients with no ill effects noted. Relief of the distention brought about striking improvement in the patient as evidenced by the clearing of the sensorium, fall in temperature and general improved comfort. With signs of impending perforation such as localized tenderness or rigidity it may be advisable to begin with very small doses or withhold the drug entirely.

SUMMARY

A series of 147 cases of typhoid fever was studied. Of the patients, forty-nine had never been immunized against the disease and the remaining ninety-eight had received two or more immunizing injections from one year to three months before contracting the disease.

The incidence was 25 per cent for nonimmunized persons and 6 per cent for the immunized. The mortality for the nonimmunized group was 10.2 per cent and for the immunized group 4 per cent.

Only 14.3 per cent of the immunized patients showed a typical typhoid course. Of the remainder, one third had an abbreviated more or less typical course while the others had a course atypical in several respects.

Constant features in order of frequency were bradycardia, splenomegaly and leukopenia.

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Clinical Notes, Suggestions and New Instruments

SOLITARY PLASMA CELL MYELOMA OF BONE AS AN INITIAL STAGE OF MULTIPLE MYELOMA

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This communication is a case report of a 41 year old man with a lesion of the trochanteric region of the right femur. It is of interest from the standpoint of diagnosis and prognosis.

Before operation the lesion of the proximal end of the right femur was felt to be a hemorrhagic bone cyst, although the possibilities of a benign or malignant bone tumor were also considered. The pathologic report on the tissue removed at operation was plasma cell myeloma of the trochanteric region of the right femur. Operation consisted of curettage and packing of the cavity with multiple small bone chips removed from the left tibia. Following operation, therapy of 1,500 roentgens was applied to the involved area. Symptoms had begun one year prior to operation. After operation and irradiation the femoral lesion appeared to remain inactive and showed x-ray evidence of progressive repair at the operative site. The patient's general condition remained good and he resumed his normal activities.

However, when he was examined four years after operation, multiple bone lesions characteristic of multiple myeloma were found.

REPORT OF CASE

L. J., a man aged 41, married, fell down a short flight of steps in November 1934, striking his right hip. Several days later he fell to the floor and again struck his right hip. After these falls he first noticed aching and pain about the upper part of the right thigh which radiated down the anterior aspect as far as the knee. The pain gradually became more severe, and on Oct. 15, 1935, eleven months after the onset of symptoms, he presented himself for examination at the New York Orthopaedic Dispensary and Hospital. His past history was essentially irrelevant, his general health having always been good. The familial history was noncontributory. Physical examination on October 26 revealed that the patient was thin and fairly well developed. He held his right lower extremity protectively. The head, neck, thorax, abdomen, upper extremities and left lower extremity were not abnormal. The blood pressure was 164 systolic, 108 diastolic, while the heart was normal clinically and no signs of decompensation were present. X-ray study of the chest revealed a sclerosed infiltration in the left infraclavicular region residual from previous pulmonary tuberculosis. The lungs were normal to percussion and auscultation. The examination of interest was confined to the right lower extremity. The legs were of equal length, but there was 1 inch atrophy of the right thigh and one fourth inch atrophy of the right calf. The right hip presented a 15 degree limitation of external rotation and a 5 degree limitation of internal rotation, as well as a moderate degree of pain and muscle spasm at the extremes of all motions. There was no swelling, tenderness or palpable deformity of the right hip or thigh.

Roentgenograms of the right femur taken on October 15 revealed an extensive lack of bone structure, in a polylocular arrangement, of the greater trochanteric area and the adjacent femoral neck and shaft. The hip joint was not involved. The lesser trochanter appeared to be separated, with a soft tissue mass beneath it. Urinalysis showed an acid reaction with a specific gravity of 1.012. A trace of albumin was present, and the urinary sediment contained amorphous urates, a few white blood cells and a few hyaline casts and cylindroids. The Bence Jones urinary protein reaction was negative prior to operation. Blood studies showed 5,250,000 red blood cells per cubic millimeter with a hemoglobin of 80 per cent. The white blood cell count was 12,300 per cubic millimeter with 71 per cent polymorphonuclear leukocytes and 29 per cent lymphocytes. The blood Kline test was negative. The erythrocyte sedimentation rate was 21 mm. at the end of one hour. The blood serum calcium level was 8.4 mg. per hundred cubic centimeters. The blood serum phosphorus was 3.2 mg. per hundred cubic centimeters, and the blood serum phosphatase was 1.4 Bodansky units per hundred cubic centimeters. The blood urea nitrogen was 15 mg. per hundred cubic centimeters, and the blood uric acid was 4.4 mg. per hundred cubic centimeters. The clinical and roentgenologic diagnosis, prior to operation, was hemorrhagic bone cyst of the proximal portion of the right femur, although the possibilities of a benign or malignant bone tumor were also entertained.

On November 1 operation was performed under nitrous oxide and ether anesthesia by Dr. James W. Toumey. A 13 cm. longitudinal incision over the lateral aspect of the proximal portion of the right thigh enabled a muscle splitting approach for a subperiostial exposure of the greater trochanter and the upper femoral shaft. An aperture 5 by 2 cm. was made through the cortex at the base of the greater trochanter, and the cyst was entered. Large connecting cystic cavities were present in the femoral neck, greater trochanter and upper femoral shaft. These cavities were partially separated by thin bony partitions. From the base of the greater trochanter the cavity extended 10 cm. up into the femoral neck and a similar distance down the shaft. The bone surrounding parts of the cysts was paper thin, especially at the junction of the neck and shaft anteriorly and posteriorly. Posteriorly there was an area 1 by 2 cm. which was devoid of bony cortex. Bleeding was severe. The cavity was filled with soft, semiliquid friable red tissue. The cortex laterally where the cyst was opened was one sixteenth inch in thickness. A frozen section of the tissue within the cavity revealed plasma cells packed together and replacing normal bone and marrow spaces. Multiple bone chips, removed with a gouge from the left tibia, were packed into the cavity after it had been thoroughly curetted of its contents. The wound was closed in layers. Because of the loss of blood at operation, a transfusion of 600 cc. of whole blood was given several hours

later. After operation the patient made an uneventful recovery. On the fourth postoperative day a long single plaster hip spica was applied to the right leg under ethylene anesthesia. Roentgenograms taken five days after operation showed the involved area to be well filled with bone chips except for the portion of the lesion lifting up the lesser trochanter, which had apparently not been reached at operation.

The material sent to the pathologic laboratory was reported as consisting grossly of numerous pieces of dark reddish soft friable tissue. On section, some pieces appeared to be old blood clot while others showed a firmer grayish homogeneous tissue interlacing as strands through the soft reddish material. There were several pieces of smooth thin cortical bone, to some of which were attached pieces of the soft tissue. Microscopically the firmer grayish soft tissue was seen to be very cellular and to have relatively little fibrous stroma. The cells, for the most part, resembled large plasma cells with prominent oval or round nuclei eccentrically placed and a considerable amount of cytoplasm. In places these cells occurred in sheets, and in other places they were scattered. The nuclear material showed coarse scattered particles often with a spokelike arrangement, and with the Unna stain a perinuclear clear zone was noted in some cells. A few mitoses were seen. There were many very thin walled vessels, some of which were closely surrounded by plasma cells.

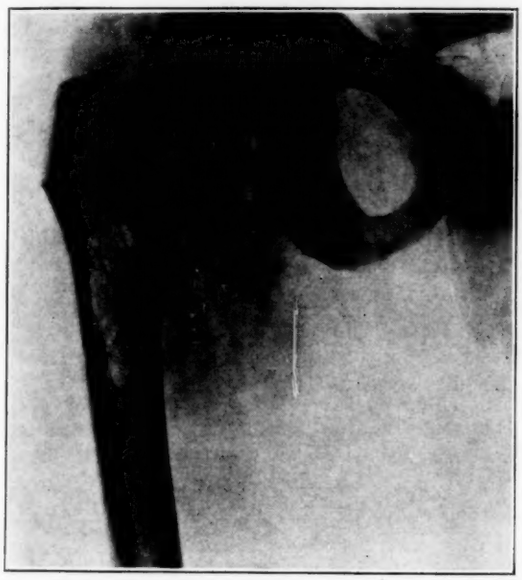

Fig. 1.—Lesion of the trochanteric region of the right femur Oct. 17, 1935, before operation and roentgen therapy. Note separation of the lesser trochanter with a soft tissue mass beneath it.

Areas of hemorrhage were present. The pathologic diagnosis made by Dr. Walker E. Swift was plasma cell myeloma. The sections were reviewed by Dr. James Ewing, of Memorial Hospital, and Dr. Robert Moore, of New York Hospital, both of whom agreed with the diagnosis. The tumor was considered to be malignant, and future local recurrence or multiple bone involvement was considered likely. It was considered to be radiosensitive.

Eleven days after operation, roentgenograms were made of the remainder of the skeleton. They revealed no additional lesions. The right femoral and left tibial wounds healed by first intention. Examination for Bence Jones protein in the urine was faintly positive five days after operation. On December 14, six weeks after operation, the patient was transferred to Memorial Hospital for roentgen irradiation of the lesion. A total of 1,500 roentgens was given over the anterior, lateral and posterior trochanteric region, 500 roentgens being given over each approach on three successive days (December 16, 17 and 18). The anterior field measured 12 by 10 cm., while the lateral and posterior fields measured 18 by 10 cm. One hundred and ninety-eight kilowatts was used through a 0.5 mm. copper filter. The tube distance was 70 cm., and 30 milliamperes was used for fifteen and one half seconds of exposure on each of the three treatments.

Three and one half months after operation the patient was allowed up in a walking plaster hip spica. In another five and one half months the spica was removed and crutches alone were used. One year later a cane was his sole support, and two years and nine months after operation this was discarded. Frequent roentgenograms revealed progressive repair at the operative site, with no recurrence of activity of the lesion and with subsidence and disappearance of the soft tissue mass in the lesser trochanteric region. Slight pain and aching about the right hip gradually subsided and the patient's general physical condition remained good.

Fig. 2.—Appearance of the lesion Nov. 18, 1939, four years after operation and roentgen therapy. Slight aching was noted about the right hip, and multiple bone lesions were discovered at this time.

The patient was last seen and examined in the follow-up clinic on Nov. 18, 1939, four years after operation. He thought his general health was quite good and he was not losing weight. However, he appeared to be chronically ill and emaciated. He was working eight hours a day as a silk cutter and was painting his house in his spare time. He had recently taken a 5 mile walk. His only complaint was a mild aching about the right hip after prolonged walking or after lying on his right side. He did not complain of symptoms other than at the right hip. Examination revealed no limitation of motion, spasm, deformity or tenderness at the right hip. Laboratory tests revealed a 1 plus Bence Jones proteinuria. Urinalysis revealed a specific gravity of 1.006, an alkaline reaction and a trace of albumin. The urinary sediment contained a few mucous threads and epithelial cells. The blood studies revealed 5,320,000 red blood cells per cubic millimeter and 78 per cent hemoglobin (12.2 Gm.). There were 10,700 white blood cells per cubic millimeter, with 83 per cent neutrophils, 15 per cent lymphocytes and 2 per cent monocytes. Fifteen per cent of the polymorphonuclear neutrophils were nonsegmented and 68 per cent were segmented. The blood serum calcium was 10.3 mg. per hundred cubic centimeters. The blood serum phosphorus was 2.9 mg. per hundred cubic centimeters, and the blood serum phosphatase was 2.5 Bodansky units per hundred cubic centimeters. Roentgenograms were again taken of the entire skeleton on November 18. They revealed no recurrence of activity at the primary lesion in the right femur. However, destructive lesions were found in the right seventh rib, the left eighth and ninth ribs, each ilium and ischium, the right tibia, the skull and the third lumbar vertebra, which were characteristic of multiple myeloma. Two weeks later he was again seen complaining of pain over the left anterior chest region. Roentgenograms revealed a pathologic fracture through a lesion in the left eighth rib.

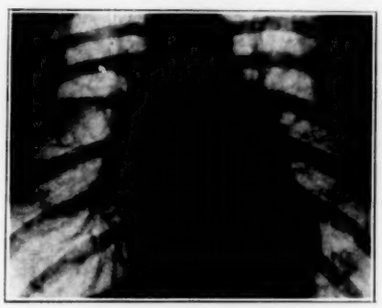

Fig. 3.—Chest plate showing lesions of the right seventh and left ninth ribs, Nov. 18, 1939. A pathologic fracture occurred through a lesion in the left eighth rib a few days later (not shown).

COMMENT

Some observers [1] feel that solitary myeloma of bone is a clinical and pathologic entity which is amenable to treatment and has a good prognosis. However, most authorities [2] believe that it is only a matter of time before a solitary myeloma of bone becomes a multiple lesion with a fatal termination. In the course of the disease such organs as the spleen, liver and kidneys may become involved.[3]

Cutler, Buschke and Cantril [4] reported twelve cases of solitary myeloma of bone from the literature and five cases from the Registry of Bone Sarcoma and added one case of their own. Of the eighteen patients, five contracted multiple lesions while under observation. Of the entire group just five were living from one to ten years after operation, their lesions supposedly having remained solitary up to that time. Six of their patients presented the lesion in the trochanteric region of the femur, as does the patient here described.

It is interesting that the Bence Jones urinary protein test was negative in this case before operation, faintly positive five days after operation and definitely positive four years after operation.

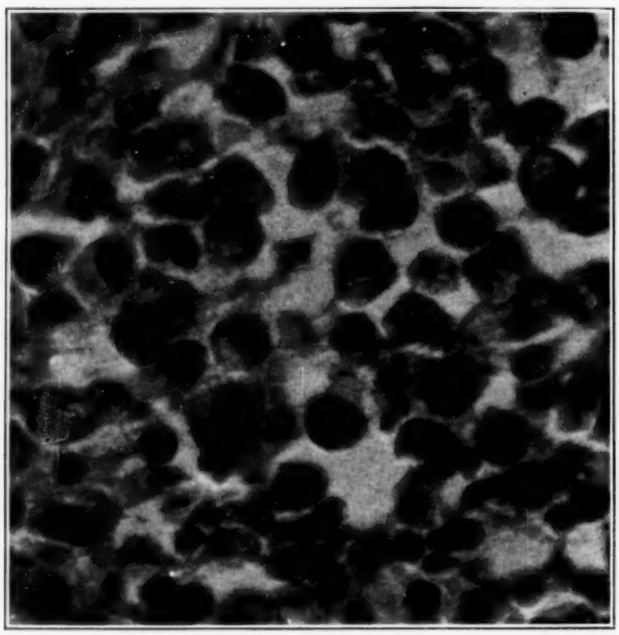

Fig. 4.—Section of tissue, × 800, curetted from the trochanteric region of the right femur. Note preponderance of plasma-like cells and scanty fibrous stroma.

SUMMARY

A multiple myeloma in a man aged 41 was thought to be either a hemorrhagic bone cyst or a tumor of the trochanteric region of the right femur before operation. Roentgenograms of the entire skeleton revealed no other lesions, and tissue section revealed that it was a plasma cell myeloma. Fifteen months after operation, roentgenograms of the chest were regarded as normal. Four years after operation and five years after onset of symptoms, multiple bone lesions were discovered. Forty-nine months after operation a pathologic fracture occurred through a lesion in the left eighth rib.

420 East Fifty-Ninth Street.

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GOUT IN A SEVENTEEN YEAR OLD GIRL

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The occurrence of gout in the young and in women is uncommon; for this reason among others the following case is reported.

REPORT OF CASE

History.—A girl aged 17 years complained chiefly of intermittent acute arthritis of the right knee of three years' duration. The family history contained one interesting feature: her mother, at the age of 20, had a uric acid stone removed from the pelvis of one kidney. She has been well since that time and has had no joint symptoms. (Her blood uric acid at present is 4.1 mg.)

The onset of the present illness was in the summer of 1936. After an 18 mile ride on a bicycle the patient began to have acute pain and swelling in the right knee. Redness was only moderate but tenderness was of extreme degree. The swelling was around the knee cap and on the sides of the knee a little below the joint. The condition was diagnosed housemaids' knee and was relieved by two weeks of rest and the use of local heat. There was no evidence of associated focal infection.

One month later the pain and swelling returned to the right knee without apparent cause. The joint disorder was considered infectious arthritis and after rest and physical therapy were instituted relief was complete.

After a few months the right knee again became swollen and very tender. On this occasion the patient was examined thoroughly and a tentative diagnosis of rheumatic fever was made. The patient was in bed one month and during the following month, after being allowed to resume activity gradually, became symptom free.

About three months later the right knee was again acutely inflamed. X-ray study revealed no abnormalities in the joint. In an attempt to eliminate foci of infection, some tonsillar remnants and adenoid tissue were removed. The leg was put in a cast for five weeks and after this the patient was on crutches for six weeks. At the end of this time roentgenograms showed decalcification to have taken place but there were no joint changes.

Following this long illness the patient became normally active and remembers no specific attacks, although she says that approximately twice a year the knee would become tender and swollen for a few days, and purgation and rest always gave rapid relief, until six weeks before admission, at which time she slipped and fell. The fall caused pain in the back and there was some swelling over the upper dorsal vertebrae. A couple of weeks later she was practicing acrobatic dancing when the right knee became painful and swollen. Laxatives were used but there was no relief, and the knee became so painful that she went to bed.

Examination.—The patient was a rather large but well proportioned and healthy looking girl. Her temperature was normal. On physical examination there were no abnormalities except those of the right knee. This knee showed a moderate amount of redness of the skin and there was slight periarticular swelling just below the knee. There was exquisite tenderness over this area. There was no limitation of motion. X-ray examination of the teeth and sinuses showed no abnormality. The white cells in the blood were not increased. The sedimentation rate of the blood was within normal limits. The uric acid content of the whole blood was 5 mg. per hundred cubic centimeters (Folin's method). Three days later it was 7 mg. and seven days later 7.5 mg. In view of the history of an intermittent "arthritis," apparently of a noninfectious type, the uric acid content of the blood and the history of a uric acid stone in the mother, a diagnosis of presumptive gout was made.

Course.—The patient was instructed to follow a diet of low purine content, and treatment was started with tincture of colchicum seed 25 drops for ten doses; this produced no diarrhea and no relief of symptoms. The blood uric acid was 7.5 mg. after the last dose. Cinchophen was then given in a dose of 0.5 Gm. six times a day for two days. On this medication the condition began to improve rapidly; the level of uric acid in the blood dropped to 5.1 mg. One week later the course of

From Emory University School of Medicine.

cinchophen was repeated and following this the blood uric acid was reduced to 3.1 mg. No further medication was given and a week later the uric acid was 3.4 mg. The patient was allowed normal activity including swimming, tennis and horseback riding, and she remained symptom free. Two months later the blood uric acid was found to be 2.8 mg., four months later 2.8 mg., six months later 3.6 mg., and now, ten months later, the patient is without symptoms and, according to her statement, in better health than she can recall in the past three years. She is still following a low purine diet and has had no further medication.

COMMENT

The emotional outlook of this girl has been changed by the diagnosis of gout and the relief of her symptoms. She had learned to dread the frequently recurring arthritis and had begun to fear a life of chronic arthritis with invalidism. Now, even though she may have a recurrence of joint pain, she will understand to some extent how to control it.

The occurrence of gout in a young girl is unusual because 98 per cent of cases of gout occur in males (Hench) and the peak in age incidence of the disease is from 40 to 50 years.

The frequency with which gout has been diagnosed in the past few years has varied in different clinics. As Hench [1] has suggested, this is due in part to the attitude of the physician, whether "conservative" or "liberal." If too conservative, early gout will not be recognized because tophi, the pathognomonic signs, are not usually present until late in the disease. The more liberal view admits that gout can be diagnosed with considerable certainty in the early stages when tophi are absent. The term "presumptive or pretophaceous gout" may be applied to such cases, following the suggestion of the American Rheumatism Association.[2] Accordingly, all gout diagnosed early must be "presumptive." Hench believes that probably 50 per cent should belong to this group. Jacobson,[3] in a study of blood uric acid, classified twelve of his twenty-one cases as "presumptive."

The diagnosis of presumptive gout can be made fairly accurately by a careful history and by studies of the uric acid content of the blood. The history is that of a recurring acute "arthritis"; during the first few years there are no symptoms between attacks and no residual joint changes. These attacks may or may not be related to excessive indulgence in food or alcohol; they are often related to trauma. There may or may not be a family history of gout. The uric acid content of the blood is usually but not always elevated in untreated cases regardless of the stage of the disease. Jacobson found the serum uric acid level in twenty-one cases of gout to be over 7 mg. per hundred cubic centimeters of blood in nineteen cases and over 6 mg. in twenty cases. Some authors have reported a lower level of uric acid in the blood in cases of true gout. Thus Monroe [4] recorded cases in which the uric acid content of whole blood was between 4.4 mg. and 6.5 mg. On the other hand an elevated uric acid content of the blood does not always mean gout, and a history of recurring acute arthritis must be present for a positive diagnosis to be made. Since the symptoms are not continuous from the onset, a chronic nonremitting arthritis with an elevated uric acid in the blood is not due to gout. To recognize gout more often one must be "gout conscious" and obtain a careful history of the attacks; to be conservative and not diagnose gout too often one must also be guided by definite criteria, which include the history, increased uric acid in the blood and, in true (later) gout, tophi.

SUMMARY

A girl aged 17 years with presumptive gout of three years' duration had a uric acid content of the blood during an attack varying from 5 to 7.5 mg. per hundred cubic centimeters.

Probably 50 per cent of gout must be classed as presumptive gout, which is pretophaceous and usually early gout.

Medical Arts Building.

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Special Article

CONFERENCES ON THERAPY

TREATMENT OF BLOOD DISORDERS

VI. PERNICIOUS AND OTHER MACROCYTIC ANEMIAS

NOTE.—*These are the actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital, with the collaboration of other departments and institutions. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Treatment of Blood Disorders: VII. Leukemia, Agranulocytosis and Neutropenia."*

DR. MCKEEN CATTELL: Dr. West, of the College of Physicians and Surgeons, has consented to introduce the discussion on macrocytic anemias.

MACROCYTIC ANEMIAS

DR. RANDOLPH WEST: Briefly, the macrocytic anemias can be conveniently classified on the basis of Castle's experiment. First, Dr. Minot found that the feeding of one-half pound (225 Gm.) of liver daily brought about improvement in patients with pernicious anemia; secondly, Castle found that by mixing normal gastric juice with beefsteak and administering that by mouth an improvement could be obtained similar to that obtained by feeding liver. Castle therefore assumed that there was in the diet an extrinsic factor which was heat stable and in the stomach juice a thermolabile factor, which he called the intrinsic factor; that these reacted together and formed the finished material, which was then absorbed and stored in the liver and released through the circulation and brought about the maturation of the marrow red cells, which then entered the circulatory blood.

Addison's pernicious anemia is due to a lack of the intrinsic factor. Almost all persons with this disease have atrophy of the mucosa of the stomach and practically no secretion of gastric juice. Secondly, there are macrocytic anemias due to a faulty diet, as exemplified in pellagra and tropical sprue, in which the diet is particularly deficient in proteins and probably in some of the accessory food elements. Thirdly, there are cases in which both the diet and the gastric juice are adequate but in which there is an impaired absorption from the intestine. This is a large factor in tropical sprue, and as the intestinal condition improves and absorption improves the anemia also improves. Fourthly, there are certain cases of Laënnec's cirrhosis in which an anemia develops which is probably due to lack of proper storage of antianemic principle in the liver. Not all cases of cirrhosis with anemia respond to liver extracts, but a certain number do, and liver therapy is worth trying. This outline gives a working classification of the macrocytic anemias, the peripheral blood picture of which you are already familiar with. The distinguishing features are, of course, large red cells well filled with hemoglobin and a color index greater than 1.

As to the treatment of these different anemias one may consider first the liver preparations available and then the stomach material. As to liver therapy, the original Minot diet contained one-half pound of whole liver daily, and its use brought about improvement of both blood and spinal cord lesions in patients suffering from pernicious anemia. Shortly afterward many

workers began the attempt to identify the material in liver which was active in pernicious anemia. Progress has been slow, as there is no test for activity except that of improvement in patients. The active material is in all probability a peptide of a molecular weight less than 10,000 and more than 5,000, as judged both by the ultracentrifuge and by passage through graded membranes. It contains none of the known vitamins. Thiamine, riboflavin and nicotinic acid are absent. It does not appear to fit into any known part of the vitamin B complex unless possibly it acts as the protein fraction which must combine with riboflavin and some of the other vitamins in order to render them active. The yellow ferment contains protein in addition to riboflavin phosphate. But that liver material may act in this way is at present mere speculation.

As soon as injectable liver preparations were available, it was found that the materials were much more active on parenteral administration than on oral administration; and while it was necessary to eat one-half pound of liver daily to get maximal blood responses, a single parenteral injection of extract obtained from as little as 10 or 20 Gm. of liver would bring about maximal responses of the blood. Therefore it was assumed that the active principle was either destroyed in the gastrointestinal tract by the various enzymes or poorly absorbed from the intestine. The material is thus from fifty to a hundred times as effective when administered parenterally as it is when administered orally. The question as to whether one substance in liver has to do with both blood and spinal cord lesions has not been settled and cannot be settled until the material is isolated in chemical purity. The purest preparations are still mixtures and not chemical entities.

That raises a point in therapy as to whether one should treat patients who have spinal cord lesions with the highly purified concentrates or whether it is desirable to use the cruder extracts possibly containing as yet unidentified factors that may influence the cord lesions. I think that most physicians prefer the crudest injectable extract for treating spinal cord involvement. If the blood alone is involved the more highly purified forms are more convenient and less painful to the patient.

The available stomach preparation has been, as you know, ventriculin, which was developed by the Ann Arbor group. They found that desiccated unheated hog's stomach when administered by mouth brought about the same improvement that was obtained with liver. They were feeding presumably both extrinsic and intrinsic factors; the muscle and the mucosa of the stomach presumably reacted just as the beefsteak and the gastric juice had done. The results have been excellent. It is necessary to feed 10 or 20 Gm. a day to bring about improvement. Some reports have appeared in the Scandinavian literature stating that stomach preparations are superior to liver in treating the cord lesions, but I think the evidence is not convincing.

The tropical macrocytic anemias of pellagra and sprue are not simply deficiencies of antianemic material alone, as you know. In pellagra the therapeutic effects of nicotinic acid and cozymase have greatly clarified this situation. All the crude liver extracts are rich in these factors, and it was observed before the isolation of nicotinic acid that very large doses of either parenteral liver extract or oral liver extract brought about improvement in pellagra. Nicotinic acid, when administered to pellagrins, has never brought about any improvement in the blood picture, and there has been no hematologic response to nicotinic acid in the anemia of pellagra or in pernicious anemia, but the blood improves when antianemic liver material is administered. There is at least a double deficiency there of antianemic material and nicotinic acid in those pellagrins who have anemia. Possibly in some cases iron too is lacking as well as other as yet undiscovered substances.

In the individuals with tropical sprue one also gets the impression of a multiple deficiency in which both liver material and other factors, some of which are known and some of which are not, are lacking, and again the cruder extracts of liver are considered much superior to the highly purified ones in the treatment of this condition.

While a really good test for absorption of liver principles from the gastrointestinal tract in man is lacking, it can be shown that the intestinal absorption of patients with sprue is at fault by their response to the various forms of liver therapy. In the old days there were numerous diets for treating tropical sprue. The gastric juice is normal in from 70 to 80 per cent of the cases, and the feeding of a high meat diet was followed by good results in perhaps 10 per cent of the cases. Dr. Ashford always used a high beef diet and at times used liver too. The impression of the group at Puerto Rico is that on a high meat diet about 10 per cent improved. With the advent of liver therapy, perhaps 25 per cent showed marked and rapid improvement in symptoms. With the introduction of crude parenteral liver extracts injected intramuscularly, improvement is obtained in 80 per cent of the cases or better. So the parenteral route has great advantages and is much more effective than the oral route owing to abnormal intestinal physiology in persons who are suffering from tropical sprue. They also almost certainly lack iron and a number of the other vitamins as well.

As to the patients with cirrhosis of the liver, we have had only a few who have responded well. Several have had reticulocyte responses and a rise in red count and hemoglobin and also have had a sense of well-being following administration of parenteral liver extract. I do not want to become involved at the moment in the treatment of cirrhosis with high vitamin diets because that is a little aside from the subject under discussion.

Perhaps the most interesting group of patients with pernicious anemia are those with spinal cord lesions, and I should also add peripheral neuritis, because there is good evidence that persons with Addison's anemia, in addition to having the usual degeneration of the pyramidal tracts and the dorsal columns, also have a spotty peripheral neuritis, and there is some evidence accumulating that they are suffering from a vitamin B_1 deficiency in addition to their other troubles. The treatment of the cord lesions is extremely important, and it is the consensus that the results are good when one is sufficiently persistent. The administration of very large amounts of liver extract every day while the patients are in the hospital, in an attempt to saturate them with it, and then after discharge the injection of large doses once or twice a week over periods of months or even years, have I think in every instance led to an arrest of the disease or to improvement. We have two men who were paralyzed from the waist down, with the bladder and rectum out of control. One had had the

disease for only about two months, while the other had had it for a number of months; but both of them have reached the point where they get up and walk about without canes or crutches, and they have been followed for three years. The effects of sufficiently persistent treatment may be extraordinary. As some one pointed out several years ago, it is imperative to make every effort to keep the blood count of the patients at or above 5,000,000, if it is at all possible to do so. In other words, those with any sign of cord lesions should be overtreated and the blood kept absolutely normal if that can be done—and in the great majority of instances it can be done.

It is certain that the cruder extracts are effective in treating this group with neurologic lesions. It is an open question whether the most highly purified extracts are. This point is being investigated by several workers but will obviously take several years to settle.

ACTION OF LIVER

I think the last and perhaps most interesting point to be discussed is the mechanism of the action of liver material, and there are one or two discrepancies in this connection that might be worth mentioning. It is known that both pepsin and trypsin can destroy the intrinsic factor. If gastric juice is incubated at a p_H of 1 or 2, the intrinsic factor is destroyed. If the juice is neutralized as soon as it is drawn, pepsin is inactivated and the intrinsic factor can be preserved for a long period of time. If trypsin is added, the intrinsic factor is again destroyed on incubation. In experiments in which beefsteak and gastric juice are incubated together at p_H 6 or 7, which is the p_H at which the intrinsic factor acts, it has not been possible to obtain a potent injectable extract. If the intrinsic factor is fed by mouth, it works very nicely. Whether or not something additional happens in the intestinal wall or at some other point is an open question.

There is one other peculiar situation. One can feed one-half pound of kidney a day, and it works just the way liver does by mouth. If, however, one prepares an extract of kidney, as with liver, one ends with no potent material at all. Presumably the active material in kidney is combined with protein and precipitated out during the first step in the purification, which is removing protein coagulable by heat. We know that the active liver material is precipitated from aqueous solution by taurocholic acid and by nucleic acid, as well as by a number of other precipitants. It is possible that the failure of the combined intrinsic and extrinsic factors to yield an injectable potent extract is analogous to the failure to obtain potent kidney extracts.

As to the mode of action of the most highly purified active liver materials, unfortunately almost nothing is known. Dr. Rhoads has advanced evidence favoring the hypothesis that it neutralizes toxic products formed in the intestine or elsewhere in the body. Some agree with that; others do not and feel that liver material corrects a deficiency. Dr. Mosenthal years ago showed (the work was reported in the *Bulletin of the Johns Hopkins Hospital* about 1916) that if patients with pernicious anemia were fed on a diet very high in nitrogen (he did not specify the type of nitrogen in the diet so we do not know whether it included liver), as they went into positive nitrogen balance the red blood count rose. Dr. Bassett, of Rochester, has done careful balance studies on patients with celiac disease and has not been able to demonstrate any improvement in the absorption of protein by the addition of liver extract to the diet. We simultaneously determined the nitrogen balance, plasma and red cell volume of a patient with macrocytic anemia, in order to see whether after the administration of parenteral liver extract the patient went into positive nitrogen balance before the blood improved or whether the blood improved before the patient went into positive balance. The result was very striking. The patient was in negative balance over the first ten day period and lost 11 Gm. of nitrogen over the nitrogen intake. There was no change in the total plasma nitrogen and there was an increase of about 50 Gm. in red blood cell nitrogen, which represented a mobilization of red cells from the bone marrow into the peripheral circulation. The liver extract released red cells from the bone marrow into the peripheral circulation, causing a measurable increase in blood nitrogen before the body as a whole went into positive nitrogen balance. So the effect of the liver extract is not primarily on nitrogen balance. Efforts to incubate cultures of bone marrow with active material have led to no significant changes so far. The fact remains that at the present time it is not known how the material acts and whether or not it fits into one of the enzyme systems.

DISCUSSION OF QUESTIONS

DR. PAUL REZNIKOFF: I wonder if you could tell the group in a few words how you treat a patient who has a relapse, how much liver extract you give and of what particular type, and how you vary the dose as the patient improves.

DR. WEST: When a patient is admitted to the hospital with a red count of 1,000,000 and no cord lesions and we want to start treatment immediately, we have been using injectable liver extracts and not the stomach preparations. The dose is stated in units, and 1 unit is defined as that amount of material which when administered daily will induce a satisfactory response in the reticulocytes, red cells and hemoglobin. We inject daily 1 cc. of an extract containing 15 units per cubic centimeter for the first week and then give it three times a week until the patient leaves the hospital. After that the dose is 1 or 2 cc. a week until the blood is normal, and then 1 cc. every one to two weeks, depending on the patient's needs. The blood is kept at the normal level. If the patient has spinal cord lesions we use the crudest injectable product containing 1 or 2 units in 3 cc. and give 3 cc. instead of the 1 cc. dose of the more highly purified product. Otherwise the plan is about the same. A weekly dose of from 3 to 6 cc. will usually maintain the blood level after it is normal and cause arrest or improvement in the cord symptoms. If these are very severe we use larger doses. In the older age groups one has to give more liver extract, and the needs of each patient vary greatly. One will need 3 cc. every three weeks; another will have to have 6 cc. a week.

DR. REZNIKOFF: How many units in 6 cc.?

DR. WEST: A dose of 6 cc. of the cruder extracts contains 12 units, so the dose is in the neighborhood of 12 units given in from one to three weeks' time. What dose do you use?

DR. REZNIKOFF: That is approximately what we use.

DR. HARRY GOLD: When do you use ventriculin?

DR. WEST: In the cases with bad cord symptoms, when we want to do everything possible, we use large doses of parenteral liver extract plus ventriculin by

mouth, always taken at the meal at which there is a slice of liver or meat. Castle's experiment calls for one-half pound of beefsteak plus 200 cc. of gastric juice every day. Reimann found that if one mixes 15 Gm. of liver (which produces no response when given daily by itself) with 15 cc. of gastric juice and administers the mixture every day, maximal responses are obtained. Liver is an excellent source of extrinsic factor in addition to finished material, and the stomach-liver preparations are probably the most potent of all. So we have tried to take advantage of that fact in bad situations by giving, in addition to the parenteral liver, a little rare liver plus ventriculin once a day or at any rate several times a week.

DR. GOLD: Gram for gram, ventriculin is more potent than liver, is it not?

DR. REZNIKOFF: Yes.

DR. WEST: For ventriculin, 20 Gm. daily is the usual dose when the blood level is low. In favorable cases 10 Gm. of ventriculin a day is effective in maintaining the blood level once it is normal.

DR. REZNIKOFF: Has anybody attempted to isolate the potent fraction from ventriculin?

DR. WEST: Nobody has yet made a potent extract of ventriculin, and nothing is known of the chemical nature of the active material in it.

DR. CLAUDE E. FORKNER: I wonder what modifications Dr. West would make in that treatment when the condition is sprue rather than pernicious anemia.

DR. WEST: In tropical sprue we would use a crude injectable extract and try to give 8 cc. a day parenterally. In addition to that we would supply a diet which is rich in all the accessory food factors. We rely on liver and brewers' yeast for our vitamin ration, assuming that in addition to those vitamins already described there are probably several more that have not been isolated yet, and they are probably present in liver or yeast.

DR. REZNIKOFF: How do you explain the good effects obtained in certain cases of pernicious anemia by Wintrobe and by Goldhammer, with large amounts of yeast alone?

DR. WEST: That raises a very nice point. Wintrobe fed 120 Gm. of dried yeast a day and had excellent responses in pernicious anemia. With liver, 250 Gm. (wet weight) is fed daily. Yeast probably contains either finished material or both intrinsic and extrinsic factors.

DR. REZNIKOFF: Goldhammer has shown that all pernicious anemia patients have some intrinsic factor and that if they are given a large amount of extrinsic factor they will, by a sort of mass action phenomenon, increase the intrinsic factor output to an effective degree. Do you think that is a tenable explanation?

DR. WEST: Yes, that is certainly one possibility. There is another interesting observation that might serve as a point of departure for further chemical work on the active materials. Normal urine given daily as a retention enema of about an ounce or so (30 cc.) to patients with pernicious anemia produces a reticulocyte response and increase in red cells and hemoglobin. The urine of patients with pernicious anemia produces the same effect, even though the donor's blood count is low. The material in urine may be simpler to work with than that in liver. However, no chemical work has been done on it.

DR. EUGENE F. DU BOIS: You said that in treating spinal cord patients you kept the red blood count at 5,000,000 or above. Is the red count in itself significant in helping directly the cord lesion or is it just an indication of something else?

DR. WEST: We have assumed that it is an indication that ample antianemic material is present in the body. It has not always been possible to maintain red cell levels at 5,000,000, but we have endeavored to do that, feeling that possibly blood had first call on what material was available and the rest went to the central nervous system. Incidentally, of the purified liver materials it is certain that a single injection of 20 mg. will give a maximal response. That is down pretty close to the vitamin dose, and Strandell has reported 2 mg. a day as giving maximal responses. That has not been confirmed, and Strandell's material which appeared on the market is a peptide too.

DR. JANET TRAVELL: Are there any toxic effects with these very large doses of liver?

DR. WEST: On giving more than one-half pound of liver a day, the symptoms of insulin shock have been noted. There is a blood sugar lowering principle in liver which has not been identified. For the extracts given in the doses that we have mentioned, I have not seen any bad effects aside from occasional reactions, with peripheral circulatory collapse occurring unpredictably.

DR. TRAVELL: With intravenous injection?

DR. WEST: No, occasionally with intramuscular injection; not more than once in two years. I do not know what the explanation is. Have you had any such reactions in the New York Hospital?

DR. REZNIKOFF: Yes, we have. On one occasion we were reasonably certain that the material entered a small blood vessel. We noticed blood at the end of the needle, although no blood appeared in the syringe before we injected the material. Another reaction we could not explain as we were reasonably certain we did not inject into a blood vessel.

DR. TRAVELL: Do the reactions tend to appear in the same person?

DR. REZNIKOFF: No, with the exception of two patients who have a fever and urticaria on every injection of liver of any type we have given them.

DR. WEST: We have not seen any urticaria.

DR. REZNIKOFF: One of our patients had a terrific reaction to purified liver extract, with a high fever and urticaria, so we never gave it to him again.

DR. WEST: We have generally switched to ventriculin by mouth or else one of the highly purified preparations if a patient has had a reaction.

DR. FORKNER: I think it should be mentioned that, although these preparations are labeled 15 units per cubic centimeter, the manufacturers fortify themselves with the statement that they contain an excess over that amount in order to be sure that there are at least 15 units in a cubic centimeter.

DR. CATTELL: Is it known whether vitamin B_1 is a factor in the improvement of the spinal cord lesions?

DR. WEST: It is hard to answer that. I think one can say this: that preparations of liver extract which are free of vitamin B_1 bring about improvement in cord lesions, but whether vitamin B_1 in addition would accelerate that process I don't know.

DR. CATTELL: Do you give additional thiamin chloride in such cases?

DR. WEST: We have not up to now, but we are thinking about it.

DR. REZNIKOFF: We have been doing it, and we have an impression that it helps in some cases.

DR. GOLD: Do you ever stop treating a patient with Addison's anemia?

DR. WEST: They often do that themselves for us, and the results have been variable. One man stopped treatment for a year or a year and a half and nothing happened at all. He was all right and had a normal blood count at the end of that time. Then in others, especially those on the verge of cord symptoms, marked spinal cord lesions will often rapidly develop.

DR. GOLD: Does the intermittent course of this disease still apply?

DR. WEST: One cannot tell now. The pattern of the disease in the preliver era was, as you know, first down and then in some instances up with several spontaneous periods of improvement, with an average prognosis of about three years. Even then transfusions made the basic pattern hard to follow.

DR. REZNIKOFF: Have you noticed that some of your patients respond to liver extract with a polycythemia, and some of them will run for a year or more with 6,000,000 red blood cells?

DR. WEST: Some have had counts above normal.

DR. TRAVELL: Without liver extract?

DR. REZNIKOFF: Continuing liver extract, but the blood level shoots way up, and when a student looks at the patient in the clinic he says he must have polycythemia.

DR. WEST: Yes, certainly some of them look like red Indians.

DR. FORKNER: Have you observed any spontaneous remissions in pernicious anemia that you thought were not due to treatment?

DR. WEST: Not since the introduction of liver. Before that we had several, but these patients had been given transfusions.

DR. FORKNER: In going over the data on spontaneous remissions in pernicious anemia, I think it is very questionable whether many patients have spontaneous remissions. Perhaps not more than 10 per cent do, and those remissions which have been recorded in the literature can almost always be explained on the basis of transfusions or the administration of arsenic or some other treatment.

DR. WEST: That is very interesting. I had not realized that.

DR. FORKNER: Prior to the introduction and use of arsenic in pernicious anemia, the incidence of remissions was in the neighborhood of 10 per cent or less; whereas after arsenic was used—as it was in almost every case up to 1926—the incidence of so-called spontaneous remissions jumped remarkably. That was first noted by Sir William Osler.

DR. REZNIKOFF: Do you know whether Dr. Fehr's case of the woman who ate pâté de foies gras every day is really authentic? It is an interesting story.

DR. WEST: I have heard the story. Her condition is supposed to have been recognized by the elder Dr. Janeway, and she outlived all her physicians. She had a passion for pâté de foies gras.

DR. FORKNER: I wonder if you would care to make any remarks about certain of these macrocytic anemias which are refractory to all types of treatment with liver and liver extract, those which seem at first to present a clinical picture somewhat like that of aplastic anemia.

DR. WEST: Another type that should have been mentioned is the anemia of pregnancy. The pregnancy group have been carefully studied in Boston and have been found to respond to liver or iron, or both. The great majority clear up after pregnancy. In a few classic Addison's anemia develops and in an occasional one aplastic anemia. Aplastic anemia also follows infections and exposure to various chemicals. Many of the refractory anemias have the hyperplastic bone marrow and not atrophic fatty marrow. One gets the impression that there are large numbers of red cells in the marrow, but they are unable to reach the peripheral circulation. So far there has been no response to liver, iron, copper or arsenic or sex hormones. Without any real evidence I have always thought of those conditions as being the analogue of an adenoma. The marrow is anatomically hyperplastic but functionally aplastic. An analogous process in a glandular organ would be an adenoma.

DR. REZNIKOFF: Have you had any patients who did not give a reticulocyte response but did show an increase of red cells with liver extract?

DR. WEST: I do not think we have had any.

DR. REZNIKOFF: They have been reported.

DR. WEST: They have been reported, but I have never seen one. Another puzzling problem is presented by the occasional patient with a million or so red cells who, while showing a 60 per cent reticulocyte response to a large dose of liver, still remains without change in the red cell count. Is there any explanation for that?

DR. FORKNER: Very careful studies show that the blood frequently goes up in steps. I think that often a case of pernicious anemia will seem to remain stationary at a level for perhaps a week or so and then suddenly show improvement. I don't know the explanation for that.

DR. REZNIKOFF: We have had patients who have responded to some degree, to 3,000,000 or 3,500,000 red cells, and then with massive doses of liver extract would go no further. We have then given those patients ventriculin, and I think in most cases we have observed good responses. What is the present status of the theories on the multiple chemical factors necessary to mature red cells? I am referring to Jacobson's work.

DR. WEST: The workers have modified their position and now hold that there are a primary factor, which is a peptide, and several accessory factors. Nobody has confirmed that. I think the peptide is in very good repute. Dakin first described it. An indipendent confirmation was made by Karrer in Switzerland, who has isolated an active mixture of peptides. For several years he thought that the phosphorus content of liver extract paralleled activity, but he got rid of the phosphorus, and the peptides were active. Strandell's material is also salted out with ammonium sulfate.

DR. TRAVELL: I should like to ask Dr. West if there are any indications for the use of iron in these macrocytic anemias.

DR. WEST: I think it has been shown that the plasma iron after the administration of liver extract actually drops during the tremendous call for iron during the synthesis of red cells; and although the body usually

has enough stored in the various organs to meet that demand, there are certainly some instances in which there is a shortage of iron in addition to liver material, and recovery will be accelerated by giving both. On the other hand, if one gives both liver and iron simultaneously, it is not possible to tell which one is effective, and the patient may continue to take liver for the rest of his life when he needs only iron. Always give one thing at a time simply from the diagnostic point of view. When the two are given together, one cannot be sure which one is effective.

DR. TRAVELL: Would you try the iron before the liver?

DR. WEST: I would decide which type of anemia the patient had and then use iron or liver first as indicated.

DR. GEORGE A. SCHUMACHER: I should like to ask a question. With malignant neoplasms anywhere in the body, except in the stomach and sometimes in the ascending colon, one frequently finds a microcytic hypochromic anemia. It is reasonable that, if there is a carcinoma in the stomach, a macrocytic anemia might develop and that would fit into your first type, but how do those anemias following neoplasms arising elsewhere fit into your classification?

DR. WEST: I simply do not know, but I think that the anemia of carcinoma of the stomach often responds to liver while the anemia of carcinoma of the ascending colon is often microcytic. Only the stomach group have been helped with liver and iron.

DR. REZNIKOFF: Only in carcinoma of the pylorus have we had fairly good results.

SUMMARY

DR. CATTELL: The therapeutic problem in the macrocytic anemias has been clarified in recent years by the recognition of the condition as a deficiency disease and the unraveling of at least some of the underlying pathologic conditions. The antianemic factor is now known to be stored in the liver. Castle's studies have shown that this substance has its source in the interaction of a heat stable substance present in meat and other protein foods (extrinsic factor) with a thermolabile material present in normal gastric juice (intrinsic factor).

Depletion of the antianemic factor occurs as the result of a number of causes, the most important being a lack of the intrinsic factor occurring in pernicious anemia, an inadequate diet giving rise to the macrocytic anemia in pellagra and tropical sprue, impaired absorption in sprue, and finally the failure to store the factor in certain cases of cirrhosis. The active material in liver has not been identified but is probably a peptide and does not correspond with any known vitamin. Various theories of its action in maintaining normal hematopoiesis have been proposed, but as yet no satisfactory proof of its role has been obtained.

The objective of treatment then is the restoration of the antianemic principle, and this is done by the administration of liver or extracts of liver. These are effective by mouth, but by this route the extracts are only from one fiftieth to one one-hundredth as potent as when given by intramuscular injection. Liver is rich in the extrinsic material as well as the finished antianemic principle and of course also certain large amounts of the various vitamins. The impression prevails that the crude extracts are more effective, especially in relation to the cord lesions, than are the more highly purified concentrates of the antianemic principle. In cases of marked involvement of the nervous system it is recommended that liver therapy be supplemented with ventriculin, a preparation of the hog's stomach containing both the extrinsic and intrinsic factors of Castle, which is very effective in producing a reticulocyte response and in maintaining the normal blood picture.

In a fully developed case of pernicious anemia an injection of 15 units of extract is given daily for the first week and then three times a week until the patient leaves the hospital. After that a dose of from 15 to 30 units is given once or twice a week until the blood is normal. The dose may usually then be reduced, most patients requiring only 15 units every one or two weeks. With cord lesions the treatment is more vigorous and the crude preparation extracts are employed, the attempt being made to maintain the red blood cells at five million or more. This treatment may be supplemented with the oral administration of liver and ventriculin, the latter in amounts of about 20 units a day with meals.

Iron is usually not required and should be withheld at least until after the effectiveness of liver therapy has been ascertained.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

BASMETER NOT ACCEPTABLE

Manufacturer: High Tension Electric Corporation, 118 West Twenty-Second Street, New York.

Many inquiries concerning the Basmeter have been addressed to the Council. The advertising referred to the Council indicated that the medical profession was being solicited actively by the manufacturer for prospective users. That the Council might fulfil its assigned function (since the product was not submitted) it procured a Basmeter on the open market for investigation and report.

According to the advertising, "The Basmeter is a new method of calculating the Basal Metabolic Rate by means of a simple slide rule principle. It eliminates the usual objections to taking a B-M-R, such as time, space, and preparation." The clinical data required for the use of the device are blood pressure, systolic and diastolic; pulse rate; respiratory rate; age; body weight. A correlating factor, "Factor J," is determined in one of the intermediate steps. The Council examined the device and compared the basal metabolic rates determined by use of the Basmeter to results obtained using established and accepted methods.

To compare the accuracy of the device, a random sample was obtained of hospital records of patients on whom blood pressure was taken at the time of the B. M. R. determination by a fully qualified and experienced technician working under the direction of a physician. The technician made the determination on all incoming patients as a part of the physical examination.

The metabolic determinations were made with an accepted instrument. Pulse rate and respiratory rate counts were for full minute periods.

These comparisons show that:

1. A most critical variation in the rates determined by the Basmeter can be produced in the results by a variation in pulse rate. This may be a change from minus 14 to plus 100 with a change in pulse rate of only one beat per minute.

2. The determination of blood pressure, which inherently is subject to a possible variation of several millimeters of mercury, can affect the calculated rate by the Basmeter in a like manner and to a similar extent.

3. The unpredictable variation of the "Factor J" with slight variations in any one of the several physical factors is apparently the main source of lack of agreement in the calculations.

The correlation between this "Factor J" under given physical conditions but varying age groups is likewise unpredictable.

A reprint sent with the device, describing the theories behind the rationale for its construction, claims close agreement between its results and hospital records—"within 1 to 1½ per cent in all but two of 1,200 cases"—yet results in the Council's survey show an agreement within 2 per cent in only ten cases of 154.

The invoice received with the device carried a typed recommendation that the user read "Standardization of Blood Pressure Readings" (THE JOURNAL, July 22, 1939, p. 294). This article not only gives definite information on methods but also states that, when careful studies of the blood pressure are to be made, the use of basal blood pressure conditions should be considered. However, although it is specified that the blood pressure should be carefully taken, in the directions for the Basmeter there is a specific claim that the Basmeter eliminates the need for omission of the morning meal and for a long period of rest.

From data compiled by the Council, it would appear that the calculation of the metabolic rate by the Basmeter gives results which are not in agreement with previously determined correlations, as will be demonstrated. Tables were compiled which were based on hypothetic but normally possible variation in single factors used by the Basmeter, the others remaining constant. These tables showed that there was an unpredictable discontinuity in basal metabolic rates, as for example:

Purely hypothetic case chosen in one of the many "critical" points on calculator: Blood pressure 170/100, age 45, weight 150 pounds, respiratory rate 22.
Pulse 74, B. M. R. — 50; pulse 75, B. M. R. + 99.

To avoid a possible criticism that the previous example is improbable, the following one is taken directly from an example in the reprint with the Basmeter:

Age 41, blood pressure 140/80, pulse rate 85, respiratory rate 16, weight 150 pounds, B. M. R. 5. Now if only the pulse is varied, the calculated results are as follows:
Pulse rate 87, B. M. R. — 37; pulse rate 84, B. M. R. — 15; pulse rate 83, B. M. R. + 35.

(Further tabular data will be included in a reprint which may be obtained from the Council on request.)

One of the graphs in the reprint accompanying the Basmeter shows the relationship of the pulse rate to the basal metabolic rate. It indicates that, roughly, there should be an increase of about 1 per cent in the basal metabolic rate for each beat per minute increase in pulse rate. Therefore the results are indisputably in conflict with one of the supposedly sound principles behind the device.

The following are direct quotations from the text of the reprint:

"No preliminaries to the test are necessary, such as the required period of rest, omission of the morning meal, etc."

"Hypertension and other causes of high blood pressure, a rapid or slow pulse or respiratory rate due to other causes besides involvement of the thyroid, obesity, etc., do not affect the reading of the basal rate on the Basmeter. The constants (Factors J) compensate for any of these changes. No individual factor such as age, weight, blood pressure, pulse rate, and respiratory rate affect the basal metabolic rate, but the combination of all the 5 factors, in relation to the constants (Factors J), give the correct basal metabolic rate."

The Council conducted a survey covering 110 cases in which the basal metabolic rates determined by use of the Basmeter were compared with those determined by use of the Aub-Du Bois standard and/or the Harris-Benedict standard. Only in ten of these cases did the rates obtained by means of the Basmeter agree within 2 per cent with the rates obtained with the standard methods, and in many cases the variation was very great. (The tabular data are omitted from this report but will be included in a reprint which may be obtained from the Council on request.)

The great discrepancy between basal metabolic rates as determined by standard methods and by the Basmeter, as well as the obvious discontinuity of results with the changing of one physical factor, would indicate that the device is subject to errors which are paradoxical in the light of the supposedly sound principles on which the design of the device is based.

The primary source of possible deviation appears to lie in the arrangement of the figures from which the "Factors J" are derived. These factors are a series of numbers for each age group, the individual factor being determined by the two divided by a hairline on the slide of the device, the two numbers being combined thus, for example: if the hairline lies between 3 and 2, the Factor J is 32. A sample of the series of numbers 1 2 8 3 2 4 3 7 3 1 2 shows that a slight movement of the slide, as for one pulse beat change, would change the Factor J in no sequential manner.

Consequently the Basmeter appears to be liable to errors not explicable in the relative magnitude of the change in factors which alter the calculated rates.

The Council on Physical Therapy voted not to accept the Basmeter for inclusion on its list of accepted devices.

AUREX HEARING AID ACCEPTABLE

Manufacturer: The Aurex Corporation, 1115 North Franklin Street, Chicago.

The Aurex Hearing Aid consists of three main components: (1) a microphone and amplifier assembly of rectangular shape, 5 by 2¼ by ⅝ inches in size and weighing 135 Gm., (2) a miniature crystal receiver with a molded soft rubber earpiece, which is three-fourths inch in diameter, one-fourth inch thick and weighs 10 Gm., and (3) a combination assembly of A and B batteries having a total weight of 304 Gm. The A battery current consumption is about 60 milliamperes and that of the B battery about 0.33 milliampere. The volume is controlled by a lever on the side of the microphone case.

Aurex Hearing Aid.

The unit was tested in a laboratory acceptable to the Council and the following were given as the procedure and results:

Internal Noise.—The internal noise is not objectionable when the earpiece is closely fitted in the ear. When this is not the case, the instrument is unstable when volume is more than three-fourths on. For the most efficient use the earpiece should be molded to fit each individual patient's ear. This observation can well be made of all hearing aids of the vacuum tube type in which the gain is high.

Amplification.—Amplification measurements were made audiometrically with two deaf subjects. The gain in decibels at the frequencies indicated, with the volume control set three-fourths on, is given in table 1.

TABLE 1.—*Amplification with Volume Control Three-Fourths On*

Frequency	128	256	512	1,024	2,048	4,096
Amplification in decibels	4	4	15	22	41	5

Amplification with the instrument set at one-half volume at the normal threshold was measured by means of tuning forks of known decay rates. These values are given in table 2.

TABLE 2.—*Amplification at One-Half Volume*

Frequency	128	256	512	1,024	2,048	4,096
Amplification at normal threshold	None	None	19	30	33	10

It should be remarked that the gain at 4,096 cycles is very markedly affected by the tightness of the fit of the auricle in the ear cavity. The gain of 41 decibels at 2,048 cycles represents a certain degree of instability of the system with a tendency to feed back at this frequency.

The Council on Physical Therapy voted to accept the Aurex Hearing Aid for inclusion on the Council's list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JULY 6, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

PHYSIOLOGICALLY ACTIVE IODIZED PROTEINS

The synthesis of a physiologically active iodine-containing protein with a specific calorigenic effect has always been assumed to be limited to the thyroid gland. The localization of almost all the iodine of the body in the thyroid and the metabolic influence of the gland have served to emphasize the relationship of the iodine-containing compounds of the thyroid to the regulation of energy metabolism. The synthesis and the degradation of thyroglobulin have been considered to be fundamental reactions under the control of the thyroid. Now come reports of the preparation of proteins of extrathyroidal origin which possess metabolic effects formerly considered to be restricted to the thyroid gland and to products derived from it. Perhaps this work will prove of fundamental importance in providing inexpensive and ready sources of thyroid-like hormone for therapeutic use. The earlier reports of Abelin and his colleagues [1] presented evidence that iodized proteins, prepared in the laboratory by the treatment of a protein with iodine, exhibited physiologic activity resembling that of thyroglobulin. These investigators conducted fractionation experiments with hydrolysates of the iodized products and succeeded in concentrating the activity in an iodine-containing fraction the chemical properties of which resembled those of thyroxine concentrates obtained from thyroid tissue. As their preparation exhibited thyroxine-like activity although they were unable to establish definitely the chemical nature of the product, Abelin and his colleagues named their active fraction "homothyroxine." More recently Ludwig and von Mutzenbecher [2] have carefully reinvestigated and expanded the investigation of the iodine compounds present in iodized products prepared in the laboratory. The latter investigators have developed the optimal conditions for the introduction of iodine into proteins and have iodized casein, serum albumin, serum globulin, silk fibroin and edestin. From each of the products, following hydrolysis, it was possible to prepare fractions which had the property of stimulating metabolism. Furthermore, it is reported that from each preparation it was possible to isolate thyroxine by further purification. Casein appeared to give the most satisfactory product from a chemical and physiologic standpoint; the serum proteins also proved to be satisfactory starting material. From the hydrolysate of iodinated casein it was possible to isolate not only thyroxine but also mono-iodotyrosine and di-iodotyrosine.

The experiments of Ludwig and von Mutzenbecher have been confirmed in both the laboratory and the clinic by investigators who, by virtue of their previous investigations, are highly qualified in the field of thyroid chemistry and physiology. Harington and Rivers [3] have treated casein with iodine under carefully controlled conditions and have obtained a product with physiologic activity similar to that of thyroglobulin and from which crystalline thyroxine was isolated. Lerman and Salter [4] report that by the iodination of serum protein they have prepared a product which produced successful responses in myxedema and cretinism and in thyroidectomized rabbits. In terms of total weight, the activity of the iodoprotein was approximately 20 per cent of that of whole thyroid; in terms of iodine content, the activity was about one four hundredth that of thyroid tissue. The artificially iodized product was hydrolyzed by alkali and by enzymes, and Lerman and Salter were able to prepare concentrates of iodine-containing products the chemical and physiologic properties of which resembled those of thyroxine and its derivates.

1. Abelin, Isaak, and Florin, A.: Arch. f. exper. Path. u. Pharmakol. **171:** 443, 1933. Abelin, ibid. **175:** 146, 151, 1934; **181:** 250, 1936. Abelin, Isaak, and Neftel, A., ibid. **189:** 473, 1938.

2. Ludwig, W., and von Mutzenbecher, P.: Ztschr. f. physiol. Chem. **258:** 195 (April) 1939. von Mutzenbecher, ibid. **261:** 253 (Oct.) 1939.

3. Harington, C. R., and Rivers, R. V. P.: Nature **144:** 205 (July 29) 1939.

4. Lerman, Jacob, and Salter, W. T.: Endocrinology **25:** 712 (Nov.) 1939.

The practical importance of having inexpensive sources of physiologically active iodine-containing products is self evident. The data which have been obtained on iodized proteins have been revealing and lead to a renewal of interest in some of the fundamental problems of thyroid physiology. A solution of the mechanism of the synthesis of thyroxine in the laboratory during the treatment of proteins with iodine may provide a possible answer to the question of the mechanism of the synthesis in the thyroid gland. The role of tyrosine and of di-iodotyrosine in this synthesis and the possible existence in proteins of thyroxine-like nuclei containing no iodine but which readily absorb this element are suggestive problems. These studies may ultimately shed light on still another fundamental problem of thyroid physiology: the specific nature of the thyroid hormone which is liberated by the thyroid gland into the circulation and which is the effective agent in accelerating the metabolic rate of the tissues.

INDUSTRIAL HEALTH AND NATIONAL DEFENSE

Modern warfare depends on industrial production. The skilled worker becomes of importance equal to that of the man under arms; his indispensability grows as it becomes difficult or impossible to replace him. Shortages are said to exist now in certain classifications of experienced craftsmen. The problem then is not solely one of educating new workers, since long periods of apprenticeship are necessary to acquire dependable ability. More important is the task of guarding the existing supply of competent and skilled workers against preventable disability. Fortunately, the medical and allied professions find themselves in better position now than in 1917 to combat causes of lost time in industry. Lessons learned in the last war about preventive industrial medicine, industrial hygiene engineering and industrial nursing have not been forgotten. Since that time technics for control over industrially induced accident or sickness have developed steadily. Trained personnel and special facilities for investigation and prevention are available in nearly all the industrial states, maintained by governmental agencies or by private industrial or insurance organizations and universities. They constitute the immediately available machinery for investigation of new occupational hazards and improved control over old ones.

Private industry also has equipped itself to protect its workers through the maintenance of medical departments. Physicians in charge of such departments are far more numerous now than formerly. They are a body of specialists in industrial practice whose equipment has progressed far beyond the relative immaturity of twenty-five years ago. In their responsible positions they act as sources of information and training for additional medical recruits. Already arrangements have been made to place at the disposal of the government the knowledge and special ability of these industrial physicians and hygienists.

Similarly the general medical profession is in a much better state of organization for specific assignments in industrial health than previously. The Council on Industrial Health has acquired information about the activities of all major medical agencies interested in the health of workers. It has conducted a census of physicians who confine their interest or give special attention to industry throughout the nation. It has investigated available facilities for industrial medical training and has arrived at conclusions about what needs to be taught both before and after graduation. At the recommendation of the Council on Industrial Health, cooperating committees in the state medical societies have been formed in the industrial areas and in a great many counties. These organized units, augmented as necessary, are available for investigations on the nature and prevalence of industrial hazards, the correlation of all local resources for control of industrial absenteeism, and the utilization of channels for professional training as well as health education for the worker. Loss of working time by skilled and indispensable workers, no matter what the cause, must be classed in war time as casualties which require mobilization of medical resources for competent handling just as do those which occur in the field. The medical profession needs to be well prepared to shoulder this special responsibility.

DESOXYCORTICOSTERONE ACETATE

In last week's issue of THE JOURNAL appeared three papers on the treatment of Addison's disease and a statement by Dr. E. S. Gordon [1] on the therapeutic status of desoxycorticosterone acetate published under the auspices of the Council on Pharmacy and Chemistry. Our knowledge of the effectiveness of this substance and the possible dangers from indiscriminate use were clearly defined. Recently the Schering Corporation, one of the manufacturers of desoxycorticosterone acetate (Cortate), has been conducting an active advertising campaign to promote the use of this substance in the prevention and treatment of surgical shock. The arguments used seem subtle. In addition to the usual selection of the favorable references in the literature, the firm has supplied physicians with blank charts entitled "Cortate Routine" on which is presented a convenient form with specific directions for the ordering of Cortate (desoxycorticosterone acetate) preoperatively and postoperatively. Actually the clinical evidence to support claims for using desoxycorticosterone acetate in the treatment of secondary shock is scanty. A number of reports have been published on the relationship between shock and the adrenal cortex in laboratory animals. Much of this work deals with a comparison of the symptoms and signs of animals that have acute adrenal insufficiency

1. Gordon, E. S.: The Use of Desoxycorticosterone and Its Esters in the Treatment of Addison's Disease, J. A. M. A. **114**: 2549 (June 29) 1940.

with those in secondary shock. Both these conditions lead to blood concentration, hypotension, subnormal temperature and asthenia. It has been also indicated that adrenalectomized animals are susceptible to trauma and other injurious processes and that adrenal cortex extracts protect such animals. None of this evidence, however, should be accepted as proof that the administration of adrenal cortex preparations is of value in clinical shock.

Most of the clinical data on which the Schering firm bases its recommendation for the use of desoxycorticosterone acetate in shock appears in a report by Perla and his associates,[2] as yet unconfirmed, on the successful prevention of surgical shock in debilitated patients who were subjected to operation. Without any criticism of the scientific value of the report by Perla, it would appear to be hardly sufficient to sustain the claims made in promotion of the product.

Confirmation of the work of Perla and his associates with evidence supported by accurate scientific studies should be awaited before routine therapeutic use is attempted. Particularly opportune at this time is the statement by the Council that desoxycorticosterone does not furnish complete replacement therapy and the warning against the indiscriminate and excessive use of this substance in routine therapy.

2. Perla, David; Freiman, D. G.; Sandberg, Marta, and Greenberg, S. S.: Prevention of Histamine and Surgical Shock by Cortical Hormone (Desoxycorticosterone Acetate and Cortine) and Saline, Proc. Soc. Exper. Biol. & Med. **43**: 397 (March) 1940.

Current Comment

A BUSINESSMAN'S APPEAL

In an address by Mr. J. Howard Pew, member of the Board of Trustees of Jefferson Medical College of Philadelphia, before the alumni dinner of that organization on June 6, he said in part: "I appeal to you men of the medical profession to come to the defense of our American system of free enterprise and equal opportunity, for the truth is that no economic planning authority could possibly have foreseen, planned, plotted and organized such an amazing spectacle of scientific, medical and industrial progress as the world has witnessed right here in America during this last century. No trust or combination, private or governmental, could have accomplished it. It could have been achieved only under conditions where there was wide-open opportunity for all the genius, inventive ability, organizing capacity and managerial skill of a great people." THE JOURNAL appreciates the compliment in this appeal. And we would appeal to American business to recognize that the regimentation of medicine would be the first insidious step in this country, as it has been in every other country in the world where it was established, toward a regimentation of all the actions of human beings. Eventually this leads to that descent into brutalism and lack of consideration for the individual human being which characterizes all totalitarian governments.

URETERO-INTESTINAL ANASTOMOSIS

In an attempt to reduce the incidence of hydronephrosis and pyelonephrosis subsequent to implantation of the ureter into the colon, Brackin,[1] experimenting with dogs, employed intact parietal peritoneum overlying the ureter in a lateral submucous uretero-intestinal anastomosis. A necrosing suture was placed in the uretero-intestinal opening; the resulting peritoneal reaction, he says, prevents leakage and tends to localize and absorb postoperative infection. The procedure was successfully accomplished in fifty-two experimental implantations in animals, after each of which a tissue necrosis occurred which resulted in a ureterosigmoidal anastomosis. In ten consecutive bilateral implantations in healthy dogs, pathologic changes in the kidneys or in the ureters were not apparent at necropsy after periods varying from three weeks to eleven months. In three animals, which died of extensive bronchial pneumonia within five days after the initial transplantation, bilateral pyelonephritis was observed. As brought out in the discussion of this paper by Walters, the difference between this type of transplantation in dogs and in human beings is significant. Since there is as yet insufficient clinical evidence of the applicability of this procedure in man, caution should be observed in applying it clinically.

1. Brackin, R. E.: A New Method of Uretero-Intestinal Anastomosis Utilizing Peritoneum, Arch. Surg. **40**: 658 (April) 1940.

PHYSIOLOGY OF CONCUSSION

It is generally agreed among fighters in the ring that it is easier to knock out an opponent by hitting a point on the lower jaw than by any other blow to the head, although it is possible by a more forceful blow to knock an opponent unconscious with a blow to almost any region of the head. In an attempt to elucidate certain aspects of the physiology of concussion, Scott[1] succeeded in demonstrating in dogs a method for recording changes in intracranial pressure produced by a blow to the head. A blow of sufficient force to cause unconsciousness results in a rise in intracranial pressure considerably above that of the systolic blood pressure. After the blow the intracranial pressure returns to the normal level and remains there. Furthermore, a loss of consciousness occurs in the dog when the intracranial pressure is raised to a level above that of the arterial blood pressure even though this pressure is maintained for only one second. Scott also demonstrated that, when the intracranial pressure does not exceed the systolic blood pressure, loss of consciousness does not occur even though the lower intracranial pressure is maintained for as long as thirty minutes. As a result of these studies, Scott feels that loss of consciousness as a result of a blow on the head may possibly be explained on the basis of short lasting, complete cerebral anemia, and he points out that this concept agrees with the previous work of Cannon and of Weiss and Baker. He further suggests that the syndrome which is known as "punch drunk" may be the result of damage to the central nervous tissue from cumulative anoxia caused by repeated, short lasting anemias produced in this manner.

1. Scott, W. W.: Physiology of Concussion, Arch. Neurol. & Psychiat. **43**: 270 (Feb.) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

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HEALTH AND MEDICAL PREPAREDNESS

THOMAS PARRAN, M.D.
Surgeon General, U. S. Public Health Service
WASHINGTON, D. C.

The problem which concerns each of us today is what we can do to contribute to the safety of our country. Traditionally, as doctors and nurses, we have been servants of peace. When war did come, it was our job to patch up the wounds, ease the suffering of the wounded, and repair as best we could the damage done by shot and shell.

We are not at war. If we have time enough—if we are swift and wise enough in the time that we have—war in this hemisphere may be prevented. But the old rules of war, and the preparation for it, have been demolished. The whole task of national defense is different from what it was twenty-five years ago. Just as the perversion of the physical and chemical sciences has brought more brutal, more rapid, more devastating destruction both to unprepared armies and to unarmed civilians, the developments of the medical sciences have expanded the scope of what doctors and public health workers can do for preparedness. The concept of a total war necessitates the concept of a total defense—a total national effort not only toward resistance but toward unassailable strength.

Psychologically, this country as yet seems unprepared for the total effort toward strength which recent world events make imperative. On the one hand we hear imprecations because we are not now better prepared in guns and ships and planes and organized manpower. On the other hand we hear criticism at steps taken now to prepare promptly against aggression toward ourselves or our immediate neighbors. One of the risks I see to national unity of action lies in the idea that defensiveness alone is all that we need to preserve our democracy. Yet, as Governor Lehman has said again and again, democracy is a thing we must constantly fight for. All recorded history shows, I think you will agree, that no nation has arisen to strength, as we have, or remained strong, as we hope to—no human rights have been established or liberties maintained—without dynamic, aggressive action. Saint Paul and the apostles were not defensive when they established the Christian faith. Our Revolutionary ancestors were not defensive when they fought to establish human liberties and found a nation. The Boston tea party, for example, was one of the most provocative acts on record. Buchanan was merely defensive when he permitted the nation to fall into the turbulence and dissension which preceded the Civil War. Lincoln took the dynamic aggressive to preserve the Union, without which we now should be as helpless as little Denmark.

REQUISITES FOR BUILDING UP NATIONAL STRENGTH

Today I would discuss with you the aggressive action which you and I, by virtue of our calling—because we are the servants of peace—must take to build up national strength. The needs to be met are enormous in scope yet simple in analysis. National strength can be built up only by the adequate application of all the sciences to the provision of armament, munitions and supplies, food and manpower. Our job is manpower.

Seven competent, trustworthy persons recently were called to assist the government in national defense. Industry is represented both in raw materials and in processing. Labor, agriculture, transportation, the consumer are represented. There is a shrewd eye on the stabilization of prices. Research problems in the physical and chemical sciences are being attacked with vigor by an able committee, which will apply all the knowledge we have or can discover to the perfection of armaments. Yet so far as I know there has been no more thought than in 1917 of the application of medical and public health science to the physical problems of a nation arming.

Yet for what cause is this nation arming if not on behalf of the men, women and children who compose it? Their physical fitness, their freedom from preventable disease, their morale or mental stamina, will determine almost entirely the effectiveness of all other defense efforts. Important in the easy days of peace without a cloud on the horizon, it is urgent now that the people of this nation be physically tough, mentally sound and morally strong. If we are not, to quote Mr. MacLeish, "we can leave our planes unbuilt and our battleships on paper. We shall not need them."

In time of stress, the health problems of the military and civilian population are inseparable. At present they are the responsibility of many unrelated federal agencies having the happiest personal good will toward one another but with no more official authority or compulsion toward coordinated action than did an airplane factory and an automobile plant two months ago. Each of these agencies legally can perform only certain functions set up by law. Each needs a closer working integration with the organized medical and public health profession. The state health departments are as diverse as the forty-eight states. None of the official agencies have the benefits of a full working relationship with the great voluntary associations for health and welfare in which doctors, dentists, nurses, engineers, in their technical capacity, work side by side with citizens to caulk up the leaks in the hull of our national man-

Read before the New York State Conference of Health Officers and Public Health Nurses, Saratoga Springs, June 25, 1940.

power. Not one of the official agencies has the full aid and service which the public spirited foundations set up to promote health and welfare are able to give.

TASKS FOR A COORDINATOR

Our defense plans, for the immediate emergency, are still young. There is much in the way of organization and coordination yet to come. But as a first step in meeting the vital needs of manpower preparedness I propose that a coordinator of medical and health preparedness for national defense be appointed under the National Defense Council. There is much for him to do. He would work with and through the Surgeon Generals of the U. S. Army, the U. S. Navy and the U. S. Public Health Service, other federal agencies, the National Research Council and the national voluntary organizations concerned with the prevention, diagnosis and treatment of disease.

A first task is the need for listing and classifying professional and technical personnel in the country; for planning and aiding, if and when necessary, the recruitment and mobilization of medical and health personnel.

Another urgent task involves the protection and promotion of the health of industrial workers. With the vast expansion of the war industries, many new industrial hazards appear and familiar ones are intensified. When new factories are designed, expert industrial hygiene advice is required for proper installation of power exhausts of chemical gases. Records of present performance show the need of extended industrial hygiene measures to control and prevent special health hazards. In the recruitment and training of workers, thorough physical examinations are necessary on employment and periodically thereafter. It is wasteful for industry to train a highly skilled employee over long months, only to have him break down suddenly with tuberculosis, mental disease or some other crippling condition. The expansion of war industries will bring acute problems of housing, medical care and health protection for workers and their families. Our industrial machines are the most efficient in the world. The men and women who man the machines must have a comparable efficiency.

DISEASES AND THEIR CONTROL

Certain diseases have particular military importance. The venereal diseases are at the top of the list. They caused more disability in the last war than anything except wounds and influenza. Fortunately we have been forehanded in building some machinery in every state to deal with this problem. We need to intensify these efforts, especially in areas of military and industrial mobilization.

The importance of tuberculosis is accentuated by the current situation. Here too we have made some progress since the last war in terms of a lower active infection rate and a lower death rate, but we do not have in any state the machinery to detect all active cases of the disease. In very few states do we have the sanatoriums to care for such cases. It should be possible promptly to find and to isolate all sources of infection. Recent developments in the small and microfilm technics mean that we can easily afford it.

Not one of the seven fine persons on the National Advisory Commission of the Defense Council, however, is aware of what this country can do to eliminate tuberculosis as a major obstacle to national security. We know that Hitler has put all of his active tuberculous together in factories to give—between dying coughs—a few months of service in munition making. This was segregation and service to the state without regard for the welfare of the individual. If we plan well now, we shall not need such suicide squads for bomb manufacture. Segregate, yes; but let us restore also.

Of the many military medical and health problems in the tropical Americas, the most important is malaria. There is no disease of comparable importance (except the mental diseases) against which we have made less scientific progress during my generation. Quinine is still the major remedy. Like rubber, originally secured from South America, now our major source of supply is from across the Pacific Ocean—the Netherland East Indies. The Netherlands is no longer able to import, process and distribute this remedy. Its cartel prevented us from storing a sufficient war chest of our most needed medical strategic material. All of Central and South America now look to us to supply their needs. For two years I have been concerned with this problem. It is not yet solved. No major military operations in the tropics of this hemisphere are possible without quinine or the equally potent German synthetic, atabrine. Here is another job for a national coordinator on the medical front.

Another strategic medical material, for which we are dependent on foreign sources, is opium. For four years I have prescribed the total annual amounts which could be imported into the United States. Before and after Munich I aided our commercial importers to build up a war chest of opium and morphine. In the vaults at Washington, formerly used to store gold, we have stored enough morphine for at least three years. Our regular source has been from the eastern Mediterranean, now closed. Before this supply is exhausted we can if necessary grow in certain areas of the United States the pain relieving poppy plant. But it must be planned now.

Other diseases require our attention. Next to the venereal diseases, mumps is the most disabling of the acute infections among recruits. Meningitis was a great hazard during the last war. Influenza still is a major threat. During the intervening twenty-two years, many facts about it are becoming clear; but, with present knowledge, effective prevention and control are not possible. Research must be speeded up and coordinated. It may be that the nation which first learns how to control influenza will by this knowledge tip the scale toward victory in the wars ahead. No one now is coordinating our search for the practical prevention of this major hazard to successful defense. Until recent months we could expect aid from medical discoveries in our sister democracies. Now in this country alone we must carry the burden. As yet we have not gone forward with it.

When armies are mobilized, certain proved immunizations are used. Typhoid fever, yes. Smallpox, yes—since Jenner's discovery of more than a hundred years ago. A recently developed toxoid against tetanus is of proved value and will be used as a routine. Effective immunization against gas gangrene would be another great aid. By a few months of coordinated effort on the part of commercial, university and governmental groups, a practical protection against this major war hazard should be perfected. Here is another job for the coordinator.

Our first concern may be in tropical America. I have discussed malaria. What about yellow fever? Prevalent throughout large areas of South America, a constant threat to the southern half of the United States, we do

not have in this country enough of the effective vaccine against it to immunize one regiment! In spite of requests from year to year, I have not been able to secure funds with which to produce a reserve supply.

These examples, among many that I could cite, illustrate my major thesis. There are many diseases, of great military importance, which we could control if we were given the will, the authority and the money to do it.

If or when war comes, every million men mobilized need 7,500 doctors drawn from civil practice. Dentists, nurses, sanitary engineers are needed too. In the mobilization of four million during the last war, more than a fourth of the effective medical men of the country were called to the colors. Whole counties were depleted of doctors. Many medical schools were almost put out of business, because the best men left for military duty. We should not repeat these mistakes. Today we should investigate who should go, who should stay to practice, to teach, to operate an essential civilian service. We have no machinery now to do this. A coordinator of medical and health preparedness should create the machinery, working with the public health agencies, the schools and the medical profession itself.

We have a shortage of laboratory technicians. Intensive courses would provide more. Universal training would deplete the ranks of medical students; yet we need doctors each year to replace obsolescence. Some medical and other scientists are vastly more valuable to the country working on their present jobs than they possibly could be in the Army or Navy. Here are other tasks for medical planning through a coordinator.

There is urgent need for standardization of many medical and surgical procedures for emergency application in time of war. Much wasted effort also could be saved through standardization of medical equipment which would be of value in civilian no less than in military practice.

THE PROBLEM OF NATIONAL FITNESS

Further, let us consider the whole problem of national fitness. The President has recommended that all youth give one year to public service—be trained during this time in some skill. How fit are they from a physical and mental point of view? Enrolment should include a careful examination. All correctable defects should receive prompt attention. As yet there is no organization, no planning of an organization to do it. This is a task projected.

Let us consider two tasks immediately before us. The National Youth Administration employs 300,000 young people. Here is a measurable group, beneficiaries of the government. After five years no plan has been worked out to appraise their physical status. Shouldn't we take this group of underprivileged youth and apply our proved medical science to relieve their correctable defects?

Employed by the Works Projects Administration are nearly two million people. The nation wants to use their services; they themselves want to serve in the ways they can best contribute to national safety. What is their physical status? No one knows. I propose that each of them be examined; that we use methods comparable to those of the draft boards of twenty-two years ago and classify the Works Projects Administration employees physically into three or four classes. Those qualified to become good workmen should be first on the list for training in the industries now short handed. Those who have remediable defects merit rehabilitation. Up to now no agency has had the authority or the money to do these two specific jobs, which seem important in national preparedness.

If our workers are malnourished, they cannot be efficient in producing what we need for defense. Yet every survey of nutrition, by whatever method conducted, shows that malnutrition in this country is widespread and serious. For example, studies by the Department of Agriculture show that 40 per cent of the people are not getting a diet adequate to maintain good health and vigor. Eight out of every ten in this category do not have an income sufficient to purchase, at market prices, a diet adequate in amount and kind; this in spite of the fact that the foods of which the nation has an apparent surplus are those in which the dietary of so many is deficient—milk and milk products, citrus fruits, green vegetables and meat.

Not through any pity for their working people, but because their scientists proved to them that it was an essential to national power, the Germans began several years ago to provide for the working masses a diet better than ours have now. We have made a beginning in this direction through the food stamp plan. What we need is an intensive national drive, with rigid scientific controls, to use the food we have to improve the fitness of our manpower.

Though I would not presume to draw up a blueprint for the whole effort of health preparedness, each of the problems mentioned needs prompt attention. With authority from the National Defense Council, several committees of experts, both official and professional, should undertake special responsibilities. What seems now a huge, illimitable job is, in reality, a composite of measurable tasks. There is a competent person to do each, if it is assigned to him. There is the will among our professions and among our citizens which will see that each is done. But, I repeat, the first step is a strong leader in the National Defense Council to see that the country's needs are met for physical and mental preparedness, for health and medical mobilization, for peace or war. At the same time he would serve to unite the efforts of official professional, commercial and voluntary groups in our unified drive for aggressive strength.

IMMEDIATE TASK OF MEDICAL SCIENCE

In the past there have been division of opinion and occasional dissension among our professions concerning methods proposed to bring better health and a higher standard of medical care to our people. In the face of danger it is the democratic way—even the herd instinct—to unite for the agreed objectives of safety. We cannot now afford controversies. The preparedness of our manpower for national safety is not controversial. Given a hand in the planning, all of us together, official and professional, can work out methods in which we all believe.

There is no time for dogged adherence to outworn patterns or for a major change in proved forms of medical practice. Medical science grows, expands, opens up new possibilities for saving life and building strength. In the application of its basic sciences, medical practice must expand also to meet the new demands of the nation for self preservation.

In the dictatorships, the state is served by sacrifice of the individual and enslavement of the men of science. If our democracy is to stand, we—as doctors, as health officers, as health workers, as citizens—of our own free will, because we know it is necessary, must put medical science to work now, fully, to make our men as good as our machines.

ORGANIZATION SECTION

PROCEEDINGS OF THE NEW YORK SESSION

MINUTES OF THE NINETY-FIRST ANNUAL SESSION OF THE AMERICAN MEDICAL ASSOCIATION, HELD IN NEW YORK, JUNE 10-14, 1940

MINUTES OF THE SECTIONS

SECTION ON PRACTICE OF MEDICINE

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2:10 by the chairman, Dr. William S. McCann, Rochester, N. Y.

Dr. Bayard T. Horton, Rochester, Minn., read a paper on "The Use of Histamine in the Treatment of Specific Types of Headaches." Discussed by Drs. Emanuel Libman, New York; Leonard G. Rowntree, Philadelphia, and Bayard T. Horton, Rochester, Minn.

Drs. James A. Greene, L. W. Swanson and Carl A. Jacobs, Iowa City, presented a paper on "The Relation of Control of Diabetes Mellitus to the Healing of Clean and Infected Wounds and to the Incidence of Infection in Clean Wounds." Discussed by Drs. Elliott P. Joslin, Boston; Roy D. McClure, Detroit, and James A. Greene, Iowa City.

Dr. Elliott P. Joslin, Boston, read the Frank Billings Lecture on "The Universality of Diabetes." Dr. Joslin was introduced by Dr. Walter L. Bierring of Des Moines, Iowa, who gave a brief historical review of the Frank Billings lectures of previous years.

Drs. Ernest E. Irons and Carl W. Apfelbach, Chicago, presented a paper on "Aspiration Bronchopneumonia with Special Reference to Aspiration of Stomach Contents." Discussed by Drs. J. P. Simonds, Chicago; William J. Kerr, San Francisco, and Carl W. Apfelbach, Chicago.

The following papers were read as a symposium on "Pulmonary Tuberculosis":

Dr. J. Arthur Myers, Minneapolis: "Epidemiology of Pulmonary Tuberculosis."

Dr. Hugh M. Kinghorn, Saranac Lake, N. Y.: "Diagnosis of Pulmonary Tuberculosis."

Dr. Ralph C. Matson, Portland, Ore.: "Treatment of Pulmonary Tuberculosis."

These three papers were discussed by Drs. Ruth E. Boynton, Minneapolis; Louis Hamman, Baltimore, and Alexius M. Forster, Colorado Springs, Colo.

THURSDAY, JUNE 13—AFTERNOON

The following officers were elected: chairman, Dr. Fred M. Smith, Iowa City; vice chairman, Dr. W. W. Palmer, New York; secretary, Dr. William D. Stroud, Philadelphia; delegate, Dr. James E. Paullin, Atlanta, Ga.; alternate, Dr. Ernest E. Irons, Chicago; member of the American Board of Internal Medicine, Dr. Reginald Fitz, Boston.

Dr. John S. Lawrence, Rochester, N. Y., read a paper on "Leukopenia: A Discussion of Its Various Modes of Production." Discussed by Drs. George R. Minot, Boston; Russell L. Haden, Cleveland, and John S. Lawrence, Rochester, N. Y.

Dr. William S. McCann, Rochester, N. Y., read the Chairman's address, entitled "Orthostatic Hypertension: The Effect of Nephroptosis on the Renal Blood Flow."

Drs. Harry Walker and William B. Porter, Richmond, Va., presented a paper on "The Clinical Syndrome Associated with Intercapillary Glomerulosclerosis." Discussed by Drs. Soma Weiss, Boston; Paul Kimmelstiel, Richmond, Va.; Sheppard Siegal, New York, and William B. Porter, Richmond, Va.

Drs. Frederick A. Willius and J. P. English, Rochester, Minn., presented a paper on "The Relation of the Use of Tobacco to Coronary Disease." Discussed by Drs. Francis D. Murphy, Milwaukee; George R. Hermann, Galveston, Texas; Soma Weiss, Boston; William D. Stroud, Philadelphia, and Frederick A. Willius, Rochester, Minn.

Drs. N. C. Gilbert, G. K. Fenn and G. V. LeRoy, Chicago, presented a paper on "The Effect of Distention of Abdominal Viscera on the Coronary Flow and on Angina Pectoris." Discussed by Drs. Lester M. Morrison, Philadelphia; C. W. Greene, Stanford University, Calif., and H. R. Miller, New York.

Drs. Herrman L. Blumgart, Monroe J. Schlesinger and Paul M. Zoll, Boston, presented a paper on "Clinical and Pathologic Studies in Coronary Artery Disease." Discussed by Drs. Fred M. Smith, Iowa City; William D. Stroud, Philadelphia, and Herrman L. Blumgart, Boston.

FRIDAY, JUNE 14—AFTERNOON

A joint meeting was held with the Section on Pharmacology and Therapeutics. The proceedings are reported in the minutes of that section.

SECTION ON SURGERY, GENERAL AND ABDOMINAL

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman, Dr. Thomas M. Joyce, Portland, Ore.

Drs. Edwin M. Miller and E. H. Fell, Chicago, and Clayton E. Brock, St. Louis, presented a paper on "Acute Appendicitis in Children: A Clinical Study of More Than 1,000 Cases."

Drs. Edward S. Stafford and David H. Sprong Jr., Baltimore, presented a paper on "An Analysis of the Mortality Resulting from Acute Appendicitis in the Johns Hopkins Hospital."

Drs. D. Woolfolk Barrow, Lexington, Ky., and Alton Ochsner, New Orleans, presented a paper on "The Treatment of Appendical Peritonitis."

These three papers were discussed by Drs. Alton Ochsner, New Orleans; E. H. Fell, Chicago; Harvey B. Stone, Baltimore; John S. Horsley Jr., Richmond, Va.; John J. Gilbride, Philadelphia, and Edwin M. Miller, Chicago.

Drs. Charles C. Lund and John H. Crandon, Boston, presented a paper on "Experimental Scurvy and Ascorbic Acid Deficiency in Surgical Patients."

Drs. John B. Hartzell, James M. Winfield and J. Logan Irvin, Detroit, presented a paper on "Plasma Vitamin C and Serum Protein Levels in Wound Disruption."

These two papers were discussed by Drs. Thomas T. Mackie, New York; Jonathan Rhoads, Philadelphia; Marshall K. Bartlett, Boston; Charles C. Lund, Boston, and John B. Hartzell, Detroit.

Dr. Elkin L. Rippy, Nashville, Tenn., read a paper on "Perforating Gunshot Wounds of the Abdomen."

Drs. Harold Price Totten and J. Norman O'Neill, Los Angeles, presented a paper on "Subcutaneous Injuries of the Abdomen."

These two papers were discussed by Drs. Adolph A. Walkling, Philadelphia; Walter E. Lee, Philadelphia; Thomas M. Joyce, Portland, Ore.; R. Arnold Griswold, Louisville, Ky.; Leo Eloesser, San Francisco; Harry E. Mock, Chicago; J. Norman O'Neill, Los Angeles, and Elkin L. Rippy, Nashville, Tenn.

THURSDAY, JUNE 13—MORNING

The following officers were elected: chairman, Dr. Lloyd Noland, Birmingham, Ala.; vice chairman, Dr. Thomas E. Jones, Cleveland; secretary, Dr. Arthur W. Allen, Boston; delegate, Dr. Fred W. Rankin, Lexington, Ky.; alternate, Dr. Hugh H. Trout, Roanoke, Va.; member of the Board of Governors, American College of Surgeons, W. Barclay Parsons, New York; member of the Board of Neurosurgery, Dr. Byron Stookey, New York.

Drs. Reed M. Nesbit and Rigdon K. Ratliff, Ann Arbor, Mich., presented a paper on "Hypertension Associated with Unilateral Kidney Infection." Discussed by Drs. E. Granville Crabtree, Boston; George W. Fish, New York; Henry A. Schroeder, New York, and Reed M. Nesbit, Ann Arbor, Mich.

Dr. Frank K. Boland, Atlanta, Ga., read a paper on "Morsus Humanus." Discussed by Drs. Michael L. Mason, Chicago; Frank L. Meleney, New York; Claude E. Welch, Boston, and Frank K. Boland, Atlanta, Ga.

Dr. Thomas M. Joyce, Portland, Ore., read the chairman's address, entitled "Combination of Old and New Methods in Repair of Inguinal Hernia."

Drs. Carrington Williams and Paul Kimmelstiel, Richmond, Va., presented a paper on "Syphilis of the Stomach." Discussed by Dr. Karl A. Meyer, Chicago.

Dr. Howard K. Gray, Rochester, Minn., read a paper on "Cancer of the Stomach with Particular Reference to the Significance of Persistent Symptoms Ascribed to the Stomach and the Malignant Potentiality of Gastric Ulcers."

Drs. Carl L. Hoag and John B. deC. M. Saunders, San Francisco, presented a paper on "Jejunoplasty for Obstruction Following Gastro-Enterostomy or Subtotal Gastric Resection."

These two papers were discussed by Drs. Alton Ochsner, New Orleans; W. Barclay Parsons, New York; Arthur W. Allen, Boston; E. E. Munger, Spencer, Iowa; Howard K. Gray, Rochester, Minn., and Carl L. Hoag, San Francisco.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Orthopedic Surgery.

Dr. John H. Powers, Cooperstown, N. Y., read a paper on "Automobile Accidents in a Rural Area Traversed by a Transcontinental Highway." Discussed by Drs. Alan DeForest Smith, New York, and John H. Powers, Cooperstown, N. Y.

Drs. James S. Speed and Harold B. Boyd, Memphis Tenn., presented a paper on "Treatment of Fractures of the Ulna with Dislocation of the Head of the Radius." Discussed by Drs. Herman F. Johnson, Omaha; Benjamin Franklin Buzby, Camden, N. J.; G. Mosser Taylor, Los Angeles; J. Albert Key, St. Louis, and Harold B. Boyd, Memphis, Tenn.

Drs. Harold C. Voris, Adrien Verbrugghen and Jerry J. Kearns, Chicago, presented a paper on "Head Injuries." Discussed by Drs. S. Bernard Wortis, New York; Donald Munro, Boston; John P. Stump, New York, and Harold C. Voris, Chicago.

Dr. Joseph S. Barr, Boston, read a paper on "The Treatment of Fracture of the External Tibial Condyle (Bumper Fracture)." Discussed by Drs. Carl E. Badgley, Ann Arbor, Mich.; Earl D. McBride, Oklahoma City, and Joseph S. Barr, Boston.

Dr. Rufus H. Alldredge, New Orleans, read a paper on "Diastasis of the Distal Tibiofibular Joint and Associated Lesions." Discussed by Drs. Clay Ray Murray, New York; George O. Eaton, Baltimore, and Rufus H. Alldredge, New Orleans.

SECTION ON OBSTETRICS AND GYNECOLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Ludwig A. Emge, San Francisco.

Drs. Richard D. Bryant and John Gwyn Fleming, Cincinnati, read a paper on "Veratrum Viride in the Treatment of Eclampsia." Discussed by Drs. Henry Lynde Woodward, Cincinnati; J. I. Hofbauer, Cincinnati, and Richard D. Bryant, Cincinnati.

The following papers were read as a symposium on "Post-pituitary Preparations in Obstetrics":

Drs. Samuel R. M. Reynolds, Brooklyn, and Douglas Power Murphy, Philadelphia: "Uterine Responses to Posterior Pituitary Substance at Term: Physiologic Considerations." Discussed by Drs. Richard Torpin, Augusta, Ga., and Sprague H. Gardiner, Baltimore.

Dr. John A. Sharkey, Philadelphia: "Should Solution of Posterior Pituitary Be Used in the First and Second Stages of Labor?" Discussed by Dr. Albert B. Davis, Camden, N. J.

Dr. George F. Pendleton, Kansas City, Mo.: "The Abuse of Solution of Posterior Pituitary During Labor." Discussed by Dr. James K. Quigley, Rochester, N. Y.

Dr. Joseph B. De Lee, Chicago: "Solution of Posterior Pituitary in Modern Obstetric Practice." Discussed by Drs. E. D. Plass, Iowa City, and E. L. King, New Orleans.

These four papers were discussed also by Drs. Douglas Power Murphy, Philadelphia; J. I. Hofbauer, Cincinnati; Rudolph W. Holmes, University, Va.; Samuel R. M. Reynolds, Brooklyn; John A. Sharkey, Philadelphia; George F. Pendleton, Kansas City, Mo., and Joseph B. De Lee, Chicago.

THURSDAY, JUNE 13—AFTERNOON

The following officers were elected: chairman, Dr. Norman F. Miller, Ann Arbor, Mich.; vice chairman, Dr. Willard R. Cooke, Galveston, Texas; secretary, Dr. Philip F. Williams, Philadelphia; representatives on American Board of Obstetrics and Gynecology, Dr. Robert D. Mussey, Rochester, Minn.; Dr. Louis E. Phaneuf, Boston, and Dr. Ludwig A. Emge, San Francisco.

Dr. Carl Henry Davis, Wilmington, Del., read a paper on "The Obstetric Forceps."

Drs. Preston T. Brown and John W. Pennington, Phoenix, Ariz., presented a paper on "Pelvic Pain of Urinary Tract Origin." Discussed by Drs. Guy L. Hunner, Baltimore, and I. W. Kahn, New York.

Drs. Gerald W. Gustafson and George J. Garceau, Indianapolis, presented a paper on "The Obstetric History of 175 Cases of Spastic Cerebral Paralysis." Discussed by Dr. Ward F. Seeley, Detroit.

Dr. B. Z. Cashman, Pittsburgh, read a paper on "The Role of Deep Cauterization in the Prevention of Cancer of the Cervix: A Report of 10,000 Cases." Discussed by Drs. Frederick C. Holden, New York; L. M. Randall, Rochester, Minn.; John J. Gilbride, Philadelphia; Morton Levin, Albany; Robert L. Dickinson, New York, and Guy L. Hunner, Baltimore.

Drs. A. N. Arneson, St. Louis, and Harry Hauptman, Jersey City, N. J., presented a paper on "Radiation in the Treatment of Carcinoma in the Body of the Uterus." Discussed by Dr. William P. Healy, New York.

Dr. Ludwig A. Emge, San Francisco, read the chairman's address, entitled "Present Trends of Socialization of Medicine in Relation to Maternal Welfare."

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Pediatrics. The proceedings are reported in the minutes of that section.

SECTION ON OPHTHALMOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman, Dr. Harry S. Gradle, Chicago.

Dr. Harry S. Gradle, Chicago, read the chairman's address.

Dr. Edward C. Ellett, Memphis, Tenn., read a paper on "Unilateral Exophthalmos."

On motion duly seconded and carried, the following resolution was adopted by the section:

WHEREAS, One state delegation has presented a resolution to the House of Delegates; and

WHEREAS, Other state medical associations have sent their recommendations direct to the section office; and

WHEREAS, The Section on Ophthalmology has been fully conscious of the needs for a new appraisal of the entire field of conservation of vision; and

WHEREAS, The House of Delegates is the legislative body of the American Medical Association; therefore, be it

Resolved, That the Section on Ophthalmology does hereby petition the House of Delegates to approve of the appointment of a Committee for the Conservation of Vision and Prevention of Blindness.

The following resolution was presented and, after discussion, was voted on and not adopted:

In view of the fact that in many parts of the country the wholesale dispensing optician has announced publicly and, on receipts given to the patient, that he is acting as the agent of the author of the prescription, the Section on Ophthalmology of the American Medical Association hereby approves of this method, which eliminates the secrecy of participation.

Drs. Frederick H. Verhoeff, Boston, and G. Victor Simpson, Washington, D. C., presented a paper on "Tubercle Within Central Retinal Vein. Hemorrhagic Glaucoma; Periphlebitis Retinalis in Other Eye." Discussed by Drs. Jonas S. Friedenwald, Baltimore; Arthur J. Bedell, Albany, N. Y.; Edward Jackson, Denver, and Frederick H. Verhoeff, Boston.

Dr. William L. Benedict, Rochester, Minn., read a paper on "Sclerocorneal Trephining." Discussed by Drs. Algernon B. Reese, New York; Manuel U. Troncoso, New York; H. Maxwell Langdon, Philadelphia; Benjamin Rones, Washington, and William L. Benedict, Rochester, Minn.

Drs. Cecil S. O'Brien and James H. Allen, Iowa City, presented a paper on "Unusual Changes in the Retinal Veins in Diabetes Mellitus." Discussed by Drs. Parker Heath, Detroit; Edward R. Thomas, Dayton, Ohio; Arthur J. Bedell, Albany, N. Y., and James H. Allen, Iowa City.

Dr. H. Maxwell Langdon, Philadelphia, read a paper on "Operations for Detachment of the Retina with Special Reference to the Use of the Thermophore." Discussed by Drs. Luther C. Peter, Philadelphia; John H. Dunnington, New York; Clyde Clapp, Baltimore; Lawrence Post, St. Louis; Oscar Wilkinson, Washington, D. C.; Harold F. Whalman, Los Angeles, and H. Maxwell Langdon, Philadelphia.

THURSDAY, JUNE 13—MORNING

Executive Session

Dr. Derrick Vail, Cincinnati, read a letter from Paris stating that field glasses were urgently needed by the French army for the purpose of distinguishing parachutists.

Dr. Derrick Vail, Cincinnati, reported that last fall a questionnaire was sent to the Fellows dealing with two resolutions regarding the optometrists and their relationship with ophthalmologists. The first resolution dealt with the ethics of the problem. The vote on that resolution to repeal was 96 and against repeal 480.

The second resolution dealt with (1) employment of optometrists by hospitals, (2) association of the members of the section with those of the optical trade, and (3) instruction of students of optometry by ophthalmologists. The vote on that resolution to repeal was 82 and against repeal 494. The executive committee of the section recommended that a subcommittee from the American Committee (Joint) on Optics and Visual Physiology be authorized to make a study and return a report with recommendations of a survey in the field of medical and nonmedical refraction.

Dr. Arthur J. Bedell, Albany, N. Y., moved that the section proceed with the action designated. The motion was seconded, voted on and carried.

Dr. Arthur J. Bedell, Albany, N. Y., reported that the resolution passed at the Wednesday morning session had been presented to the Board of Trustees, which requested the following addition to the resolution: "Who shall be responsible to the Board of Trustees of the American Medical Association. It shall collect data showing the status of conservation measures in each state; shall act as a clearing house for all information regarding conservation of vision and prevention of blindness but shall make no pronouncement on policy or rules until approved by this section."

On motion, duly seconded, the amendment was adopted.

Dr. Albert C. Snell, Rochester, N. Y., read the report of the Committee on Visual Economics, with the following recommendations:

1. That the committee be continued and that its membership be increased to three.

2. That the committee be requested to revise the report of 1925 and that a revised report be prepared, published and sent to all members of this section one month before the next annual meeting, and that the revision be made a matter of special consideration at the 1941 meeting. The report was adopted.

Dr. Walter B. Lancaster, Boston, read the report of the American Committee (Joint) on Optics and Visual Physiology (representing the Section on Ophthalmology of the American Medical Association). The report was accepted.

Dr. Parker Heath, Detroit, Treasurer, read the report of the Committee on Knapp Testimonial Fund. The report was accepted.

Dr. Frederick H. Verhoeff, Boston, reported for the Committee on Awarding the Knapp Medal as follows: Including the first award in 1914, the Knapp Medal has been awarded only seven times in the past twenty-six years. It is evident, therefore, that previous committees have attempted to set a very high standard for subsequent papers to compete against. Each member of the present committee, justly or unjustly, has been awarded the medal, and this fact, for reasons that need not be specified, raised the hurdle to be surmounted by the papers read last year. In spite of these facts, the committee found the paper to be of immensely high merit. The committee unanimously and without any hesitation decided that one paper in every respect not only met but exceeded its requirements. This was the paper entitled "Primary Tumors of the Optic Nerve (A Phenomenon of Recklinghausen's Disease)" written by Dr. Frederick Allison Davis, Madison, Wis. Dr. Davis accepted the medal and expressed his appreciation.

Dr. Derrick Vail, Cincinnati, read the report of the Committee on National Museum of Ophthalmic Pathology. The report was accepted.

Dr. Derrick Vail, Cincinnati, read the report of the Exhibit Committee of the Section. The report was accepted.

Dr. Arthur J. Bedell, Albany, N. Y., reported as delegate of the section to the House of Delegates.

Dr. S. Judd Beach, Portland, Maine, read the report of the Committee on American Ophthalmology.

Dr. Derrick Vail, Cincinnati, read the report of the Committee on Museum of Ophthalmic History.

The report of the Committee on American Orthoptic Council was read by Dr. Derrick Vail, Cincinnati, the chairman.

Dr. William L. Benedict, Rochester, Minn., reported for the Advisory Committee on Student Health Council that a specially designed vision test chart holder had been approved for the use of the Eye Health Committee in examination of college students; that a complete record system for the recording of results of examination of the eyes of college students made under the auspices of the Eye Health Committee had been approved and is now in operation in all colleges that belong to this organization. The committee recommended that it be continued. The report of the committee was accepted.

Dr. Parker Heath, Detroit, read the report of the Committee on Ophthalmic Literature. The report was accepted, with the recommendation that the committee be continued.

The following committee for awarding the Knapp Medal for 1940 was elected from the floor: Dr. Walter B. Lancaster, Boston; Dr. Sanford R. Gifford, Chicago, and Dr. Bernard Samuels, New York.

The following officers were elected: chairman, Dr. Albert C. Snell, Rochester, N. Y.; vice chairman, Dr. Edwin M. Neher, Salt Lake City; secretary, Dr. Derrick Vail, Cincinnati; executive committee: Dr. S. Judd Beach, Portland, Maine; Dr. Harry S. Gradle, Chicago, and Dr. Albert C. Snell, Rochester, N. Y.; delegate, Dr. Arthur J. Bedell, Albany, N. Y.; alternate, Dr. Shaler A. Richardson, Jacksonville, Fla.

The following committee appointments were recommended by the executive committee and approved:

Reelection for three years of Dr. William H. Luedde, St. Louis, to the American Committee (Joint) on Optics and Visual Physiology.

Reelection for four years of Dr. S. Judd Beach, Portland, Maine, to the American Board of Ophthalmology.

To the Committee of National Museum of Ophthalmic (Joint) Pathology, Dr. Jonas S. Friedenwald, Baltimore.

Reelection of Dr. Georgiana Dvorak Theobald, Oak Park, Ill., to fill the vacancy of chairman of the Committee for Scientific Exhibit from the Section. The appointment of Dr. Derrick Vail, Cincinnati, and Dr. John E. L. Keyes, Youngstown, Ohio, to the committee.

The election of Dr. Robert Von der Heydt, Chicago, Dr. Burton Chance, Philadelphia, Dr. J. W. Jervey, Greenville, S. C., and Dr. Hans Barkan, San Francisco, to constitute the Committee on Museum of Ophthalmic History.

Election for three years of Dr. Maynard C. Wheeler, New York, to fill a vacancy on the American Council on Orthoptics.

To the Advisory Committee of Student Health Association, the reelection of Dr. William L. Benedict, Rochester, Minn.

To discontinue the committee from the Section to Cooperate with the National Committee for the Prevention of Blindness.

To continue for one year the present Committee on Ophthalmic Literature (Joint).

The election of Dr. Alfred Cowan, Philadelphia, to the Committee on Visual Economics.

Scientific Session

Dr. Alan C. Woods, Baltimore, read a paper on "The Effect of Sensitivity and Immunity on the Experimental Lesions of Ocular Tuberculosis." Discussed by Drs. Edwin W. Burton, Charlottesville, Va.; Merrill J. King, Boston, and Alan C. Woods, Baltimore.

Dr. Alson E. Braley, Detroit, read a paper on "Intracellular Bodies of the Conjunctival Epithelial Cells." Discussed by Drs. Phillips Thygeson, New York, and Alson E. Braley, Detroit.

Dr. Albert E. Sloane, Boston, read a paper on "Massachusetts Vesion Test: An Improved Method of School Eye Testing." Discussed by Drs. S. Judd Beach, Portland, Maine; Maynard C. Wheeler, New York; S. Weir Newmayer, Philadelphia; Edward Jackson, Denver, and Albert E. Sloane, Boston.

Demonstration Session

Dr. Dikran M. Yazujian, Trenton, N. J., presented an apparatus for localizing intra-ocular foreign bodies.

Dr. Albert E. Sloane, Boston, presented experimental apparatus for the Massachusetts vision test.

Dr. Walter B. Lancaster, Boston, demonstrated some magnets.

Dr. Conrad Berens, New York, presented muscle forceps without teeth; a curved glaucoma knife; a cataract knife.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Nervous and Mental Diseases.

Executive Session

Dr. Arthur J. Bedell, Albany, N. Y., reported as delegate to the House of Delegates that the resolution of the section was unanimously adopted by the House of Delegates.

Dr. Henry R. Viets, Boston, reported as delegate to the House of Delegates from the Section on Nervous and Mental Diseases that the resolution dealing with the endorsement of the Central Neuro-Psychiatric Institute as proposed by the United States Public Health Service failed of passage in the House; that the resolution dealing with the so-called Pennsylvania Plan of training in legal psychiatry was tabled. Dr. Viets suggested that the section itself have a committee to consider resolutions, and that the resolutions be put in the first day of the meeting and referred to a committee of the section.

Scientific Session

Dr. Walter E. Dandy, Baltimore, read a paper on "Results Following the Intracranial Approach for Orbital Tumors." Discussed by Drs. Arnold Knapp, New York; William L. Benedict, Rochester, Minn., and Walter E. Dandy, Baltimore.

Drs. Ward C. Halstead and A. Earl Walker, Chicago, presented a paper on "Sparing and Nonsparing of 'Macular' Vision Associated with Occipital Lobectomy in Man." Discussed by Drs. Wilder G. Penfield, Montreal; P. J. Leinfelder, Iowa City; Tracy J. Putnam, New York; W. Ivan Lillie, Philadelphia, and A. Earl Walker, Chicago.

Dr. Albert D. Ruedemann, Cleveland, read a paper on "Comparison of Differential Diagnosis of Brain Lesions by Visual Fields, Encephalography and Ventriculography." Discussed by Drs. John N. Evans, Brooklyn, and Albert D. Ruedemann, Cleveland.

Dr. Francis H. Adler, Philadelphia, read a paper on "Primary Pituitary Adenomas and the Syndrome of the Cavernous Sinus." Discussed by Drs. William J. German Jr., New Haven, Conn.; Oscar Hirsch, Boston, and Francis H. Adler, Philadelphia.

Dr. W. Ivan Lillie, Philadelphia, read a paper on "Prechiasmal Syndrome Produced by Chronic Local Arachnoiditis." Discussed by Drs. Temple S. Fay, Philadelphia; Derrick Vail, Cincinnati, and W. Ivan Lillie, Philadelphia.

Drs. Robert B. Aird and Howard C. Naffziger, San Francisco, read a paper on "The Myopathy and Etiology of Exophthalmos Experimentally Produced by Extracts of the Anterior Pituitary." Discussed by Drs. David Marine, New York; Harry B. Friedgood, Boston; Derrick Vail, Cincinnati, and Robert B. Aird, San Francisco.

SECTION ON LARYNGOLOGY, OTOLOGY AND RHINOLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Arthur W. Proetz, St. Louis.

Dr. Leon Felderman, Philadelphia, read a paper on "Ethmosphenoidal Epiglottidean Syndrome Interfering with Vocal Range." Discussed by Drs. James S. Greene, New York; Irving W. Voorhees, New York, and Leon Felderman, Philadelphia.

Dr. Mercer G. Lynch, New Orleans, read a paper on "Geographic Virulence of Mastoiditis." Discussed by Drs. Noah D. Fabricant, Chicago; Lester A. Brown, Atlanta, Ga., and Mercer G. Lynch, New Orleans.

Dr. Frederick T. Hill, Waterville, Maine, read a paper on "Diagnostic Pitfalls in the Nasopharynx."

Dr. Frederick A. Figi, Rochester, Minn., read a paper on "Fibromas of the Nasopharynx."

These two papers were discussed by Drs. Joseph D. Kelly, New York; Charles J. Imperatori, New York; Gordon B. New, Rochester, Minn.; Frederick T. Hill, Waterville, Maine, and Frederick A. Figi, Rochester, Minn.

Dr. Harold A. Fletcher, San Francisco, read a paper on "Industrial Aspects of Ear, Nose and Throat Practice." Discussed by Drs. W. E. Grove, Milwaukee; H. A. Kuhn, Hammond, Ind.; Walter F. Schaller, San Francisco; Rea E. Ashley, San Francisco, and Harold A. Fletcher, San Francisco.

Dr. W. Likely Simpson, Memphis, Tenn., read a paper on "Osteoma of the Mastoid Process." Discussed by Dr. George M. Coates, Philadelphia.

THURSDAY, JUNE 13—AFTERNOON

Executive Session

The following officers were elected: chairman, Dr. LeRoy A. Schall, Boston; vice chairman, Dr. W. E. Grove, Milwaukee; secretary, Dr. Louis H. Clerf, Philadelphia; executive committee: Dr. H. Marshall Taylor, Jacksonville, Fla.; Dr. Arthur W. Proetz, St. Louis, and Dr. LeRoy A. Schall, Boston; delegate, Dr. Burt R. Shurly, Detroit; alternate, Dr. Gordon F. Harkness, Davenport, Iowa.

Dr. H. Marshall Taylor, Jacksonville, Fla., reported that the Committee on Swimming had no report to make and asked that the committee be discharged. On motion, duly seconded and carried, the committee was discharged, with thanks.

Scientific Session

Dr. Arthur W. Proetz, St. Louis, read the chairman's address, entitled "The Functional Point of View in Rhinology."

Dr. J. MacKenzie Brown, Los Angeles, read a paper on "The Treatment of Acute and Chronic Sinus Disease."

Dr. Harold I. Lillie, Rochester, Minn., read a paper on "The Treatment of Acute and Chronic Otitis Media."

Dr. Lyman G. Richards, Boston, read a paper on "The Treatment of Diseases of the Throat."

An open forum with questions from the floor was held on these three papers.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Radiology. The proceedings are reported in the minutes of that section.

SECTION ON PEDIATRICS

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:10 by the chairman, Dr. Albert D. Kaiser, Rochester, N. Y.

Dr. F. M. Pottenger Jr., Monrovia, Calif., read a paper on "The Role of Nutrition in the Production of Childhood Asthma." Discussed by Drs. W. Ambrose McGee, Richmond, Va., and F. M. Pottenger Jr., Monrovia, Calif.

Dr. Frank Lee Bivings, Atlanta, Ga., read a paper on "Asthmatic Bronchitis Following Chronic Upper Respiratory Infection." Discussed by Drs. Hal M. Davison, Atlanta, Ga.; Warren W. Quillian, Coral Gables, Fla.; Harry Lowenburg Jr., Philadelphia, and Frank Lee Bivings, Atlanta, Ga.

A committee on resolutions was appointed by the chairman, composed of Drs. John Aikman, Rochester, N. Y.; Victor J. Greenebaum, Cincinnati, and Gilbert J. Levy, Memphis, Tenn.

Drs. Clifford D. Sweet, Lawrence R. Jacobus and Henry E. Stafford, Oakland, Calif., presented a paper on "Child-Parent Relationships." Discussed by Drs. Oscar Reiss, Los Angeles; I. Edward Liss, New York, and Clifford D. Sweet, Oakland, Calif.

Drs. F. W. Schlutz and Elizabeth M. Knott, Chicago, presented a paper on "Factors Which Affect the Level of Vitamin B_1 in the Blood of Infants and Children." Discussed by Dr. Herbert Pollack, New York.

Dr. Lee Forrest Hill, Des Moines, Iowa, read a paper on "Scope of the Health Examination for Well Children," which was followed by a talking picture, "Bobby Goes to School."

THURSDAY, JUNE 13—MORNING

Dr. John Aikman, Rochester, N. Y., chairman of the resolutions committee (which also serves as the executive committee), presented the following resolutions, which, on motion regularly made and seconded, it was voted to approve:

Resolved, That in the death of Dr. John Lovett Morse the Section on Pediatrics of the American Medical Association and the pediatric profession of the United States have lost an outstanding pioneer, leader and teacher. Dr. Morse at all times gave freely of himself to the advancement of pediatrics and has left an indelible influence on pediatrics in America. His loyalty and his contributions to this section have been invaluable.

Resolved, That this motion be placed in the minutes of the Section on Pediatrics and that a copy be sent to the family of Dr. Morse.

Resolved, That the Section on Pediatrics extends thanks and appreciation to Dr. Adolf De Sanctis and his committee for the generous hospitality and many courtesies shown to the section during this meeting.

The committee also moved that a telegram be sent to Dr. Edward Clay Mitchell, Memphis, Tenn., member of the executive committee, expressing disappointment in his absence during the meeting and wishing him a speedy recovery from his illness. This motion was seconded, put to a vote and carried.

The chairman called attention to the fact that an index to the AMERICAN JOURNAL OF DISEASES OF CHILDREN was dependent on the number of demands for such an index and urged that members desiring the index communicate with Dr. Clifford G. Grulee, Evanston, Ill., who was in charge of this work.

The following officers were elected: chairman, Dr. Julius H. Hess, Chicago; vice chairman, Dr. John A. Toomey, Cleveland; secretary, Dr. Hugh L. Dwyer, Kansas City, Mo.; delegate, Dr. William Weston, Columbia, S. C.; alternate, Dr. A. Graeme Mitchell, Cincinnati; executive committee: Dr. John Aikman, Rochester, N. Y.; Dr. J. Victor Greenebaum, Cincinnati, and Dr. Gilbert J. Levy, Memphis, Tenn.; representative in charge of the scientific section, Dr. Arthur F. Abt, Chicago.

The chairman reported for the Abraham Jacobi Fund in the absence of the secretary, stating that $22.53 had been added to the fund during the year; also on June 12 a payment of $481 had been authorized to cover the landscaping and planting of the grounds around Dr. Jacobi's grave in Bolton Landing, N. Y., and a further amount, not to exceed $75, for the maintenance of the grounds each year; also that the sum of $1,500 which had been authorized for the fifth International Congress of Pediatrics which was to have been held in Boston in 1940 and which meeting had been indefinitely postponed, was to be restored to the fund until such time as such a meeting could be held.

The chairman also reported the suggestion of the secretary that each year some one be invited to address the Section on Pediatrics as an Abraham Jacobi lecturer, the amount of money to be spent on this as an honorarium to the lecturer not to exceed $100. The amount in the Abraham Jacobi Fund at the present time amounted to $7,500.

Dr. Albert D. Kaiser, Rochester, N. Y., read the chairman's address, entitled "Significance of the Tonsils in the Development of the Child."

The following papers were read in a Panel Discussion on Some Contagious Diseases, during which Dr. John A. Toomey, Cleveland, presided:

Erling S. Platou, Minneapolis: "Convalescent Serums."

Dr. Gladys Henry Dick, Chicago: "Scarlet Fever: Active and Passive Immunity."

Dr. Conrad Wesselhoeft, Boston: "Nephritis in Scarlet Fever and Its Treatment."

Dr. Charles F. McKhann, Boston: "Measles Prevention."

Dr. Archibald L. Hoyne, Chicago: "Treatment of Epidemic Meningitis."

Dr. Louis W. Sauer, Evanston, Ill.: "Active Immunity in Whooping Cough."

Dr. Joseph Stokes Jr., Philadelphia: "Epidemic Influenza: Diagnosis."

Dr. John A. Toomey, Cleveland: "Differential Diagnosis of Various Forms of Encephalitis."

Following the presentation of these papers, questions were submitted by the members of the section and answered by the particular member of the panel to whom they were directed.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Obstetrics and Gynecology.

Dr. Priscilla White, Boston, read a paper on "Prediction and Prevention of Pregnancy Accidents in Diabetes."

Dr. Warren R. Sisson, Boston, read a paper on "The Neonatal Problem in Infants of Diabetic Mothers."

These two papers were discussed by Drs. J. A. Lamphier, Brooklyn, and Priscilla White, Boston.

Dr. Edith L. Potter, Chicago, read a paper on "A Study of Fetal and Neonatal Deaths: A Statistical Review." Discussed by Drs. Ludwig A. Emge, San Francisco, and Edith L. Potter, Chicago.

Drs. Ethel C. Dunham and Jessie M. Bierman, Washington, D. C., presented a paper on "The Care of the Premature Infant." Discussed by Drs. Harry Lowenburg, Philadelphia, and Ethel C. Dunham, Washington, D. C.

Dr. Julius H. Hess, Chicago, read a paper on "The Responsibilities of the Newborn Service from the Standpoint of the Pediatrician."

Dr. W. W. Waddell Jr., Charlottesville, Va., read a paper on "Vitamin K in the Prevention and Treatment of Prothrombin

Deficiency and Associated Hemorrhage in the Newborn." Discussed by Drs. Clifford D. Sweet, Oakland, Calif.; Chester R. Brown, Arlington, N. J., and W. W. Waddell Jr., Charlottesville, Va.

SECTION ON PHARMACOLOGY AND THERAPEUTICS

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:05 by the chairman, Dr. Irving S. Wright, New York.

Drs. Verne W. Swigert, Evanston, Ill., and Reginald Fitz, Boston, presented a paper on "The Effect of Mersalyl (Salyrgan) on Plasma and Blood Volume." Discussed by Drs. Leonard G. Rowntree, Philadelphia; Maurice Bruger, New York; George R. Herrmann, Galveston, Texas., and Verne W. Swigert, Evanston, Ill.

Drs. Meyer Bodansky, J. L. Jinkins, H. Levine and A. J. Gilbert, Galveston, Texas, presented a paper on "Clinical and Experimental Studies on Paraldehyde." Discussed by Drs. S. Bernard Wortis, New York; Norman H. Jolliffe, New York; Reginald Fitz, Boston, and Meyer Bodansky, Galveston, Texas.

Dr. M. I. Smith, Washington, D. C., read a paper entitled "A Review of the More Recent Field and Laboratory Studies in Chronic Selenium Poisoning." Discussed by Dr. J. H. Sterner, Rochester, N. Y.

Drs. Bernard M. Jacobson and Yellapragada Subbarow, Boston, presented a paper on "Studies of the Principle in Liver Effective in Pernicious Anemia: VI. Recent Advances in the Purification of Active Substances." Discussed by Drs. Randolph West, New York; W. T. Salter, Boston, and Bernard M. Jacobson, Boston.

Drs. Charles Mazer, S. Leon Israel and Elkin Ravetz, Philadelphia, presented a paper on "An Experimental and Clinical Evaluation of the Synthetic Estrogen Stilbestrol." Discussed by Drs. Theodore Neustaedter, New York; L. M. Randall, Rochester, Minn.; A. A. Herold, Shreveport, La., and Charles Mazer, Philadelphia.

Drs. Joseph B. Kirsner and Walter L. Palmer, Chicago, presented a paper on "The Role of Chlorides in the Treatment of Alkalosis." Discussed by Drs. Dana W. Atchley, New York; L. C. Gatewood, Chicago; E. N. Collins, Cleveland, and Joseph B. Kirsner, Chicago.

THURSDAY, JUNE 13—MORNING

The chairman reported to the section the recommendation of the executive committee that the name of the section be changed to Section on Therapeutics and Experimental Medicine. On the motion of Dr. Joseph B. Wolffe, Philadelphia, it was unanimously voted that this change be recommended to the House of Delegates.

The following officers were elected: chairman, Dr. C. M. Gruber, Philadelphia; vice chairman, Dr. Wallace M. Yater, Washington, D. C.; secretary, Dr. Edgar V. Allen, Rochester, Minn.; delegate, Dr. Irving S. Wright, New York; alternate, Dr. O. P. J. Falk, St. Louis; executive committee: Drs. Erwin E. Nelson, New Orleans; Irving S. Wright, New York, and C. M. Gruber, Philadelphia.

Dr. Irving S. Wright, New York, read the chairman's address, entitled "Social Significance and Ultimate Objective of the Treatment of Arteriosclerosis Obliterans."

Drs. James G. Carr, Alexander Sanders and Gilbert H. Marquardt, Chicago, presented a paper on "The Treatment of Angina Pectoris by Pancreatic Tissue Extract." Discussed by Drs. A. Wilbur Duryee, New York; Emanuel Libman, New York; T. K. Lewis, Birmingham, Ala.; Joseph B. Wolffe, Philadelphia; Anna Samuelson, New York; John F. Casey, Boston, and Gilbert H. Marquardt, Chicago.

Dr. Jerome W. Conn, Ann Arbor, Mich., read a paper on "The Spontaneous Hypoglycemias: The Importance of Etiology in Determining Treatment." Discussed by Drs. Herbert Pollack, New York; E. J. Kepler, Rochester, Minn.; G. M. Churukian, Paris, Ill., and Jerome W. Conn, Ann Arbor, Mich.

Dr. A. R. MacLean, Rochester, Minn., read a paper on "The Treatment of Orthostatic Hypotension and Orthostatic Tachycardia." Discussed by Drs. Horace Korns, Iowa City; O. P. J. Falk, St. Louis, and A. R. MacLean, Rochester, Minn.

Dr. William P. Murphy, Boston, read a paper entitled "A Note of Optimism in the Treatment of the Patient with Chronic Leukemia." Discussed by Drs. Irving S. Wright, New York; H. J. Ullmann, Santa Barbara, Calif.; Paul Reznikoff, New York; Claude E. Forkner, New York, and William P. Murphy, Boston.

Drs. E. N. Collins, Cleveland, C. P. Pritchett, Columbus, Ohio, and H. R. Rossmiller, Cleveland, presented a paper on "The Use of Aluminum Hydroxide in the Treatment of Peptic Ulcer." Discussed by Drs. James Flexner, New York; Arthur J. Atkinson, Chicago; I. H. Einsel, Cleveland; Manfred Kraemer, Newark, N. J.; Isidor Greenwald, New York, and E. N. Collins, Cleveland.

Drs. Harrison F. Flippin, Leon Schwartz and John G. Reinhold, Philadelphia, presented a paper on "Sulfathiazole and Sulfapyridine Therapy in Pneumonia." Discussed by Drs. Herbert K. Ensworth, New York; Elmer H. Loughlin, Brooklyn; John F. Casey, Boston, and Harrison F. Flippin, Philadelphia.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Practice of Medicine.

Drs. Francis D. Murphy, Milwaukee, Howard L. Correll, Wauwatosa, Wis., and John C. Grill, Milwaukee, presented a paper on "The Effects of Intravenous Solutions on Patients With and Without Cardiovascular Defects." Discussed by Drs. N. C. Gilbert, Chicago, and Irvine H. Page, Indianapolis.

Drs. Arthur Grollman, Baltimore, and J. R. Williams Jr. and T. R. Harrison, Nashville, Tenn., presented a paper on "The Antipressor Action of Renal Extracts." Discussed by Drs. J. Murray Steele, New York; M. C. Winternitz, New Haven, Conn.; Edgar V. Allen, Rochester, Minn.; Frederick M. Allen, New York; Benjamin Jablons, New York, and T. R. Harrison, Nashville, Tenn.

Dr. Paul Padget, Baltimore, read a paper on "Long-Term Results in the Treatment of Early Syphilis." Discussed by Dr. Joseph Earle Moore, Baltimore.

Drs. Wallace E. Herrell and Alex E. Brown, Rochester, Minn., presented a paper on "The Treatment of Septicemia: Results Before and Since the Advent of Sulfamido Compounds." Discussed by Drs. Perrin H. Long, Baltimore, and Wallace E. Herrell, Rochester, Minn.

SECTION ON PATHOLOGY AND PHYSIOLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2:05 by the chairman, Dr. Frank W. Hartman, Detroit.

The following papers were read as a symposium on "Anoxia":

Dr. Ernst Gellhorn, Chicago: "Fundamental Principles in the Adjustment Reactions of the Organisms to Anoxia."

Dr. Carl J. Wiggers, Cleveland: "Cardiac Adaptations During Anoxia."

Dr. H. E. Himwich, Albany, N. Y.: "Anoxia and the Treatment of Schizophrenia."

Dr. Ralph M. Waters, Madison, Wis.: "Anoxia from the Anesthetist's Point of View."

Dr. Nicholson J. Eastman, Baltimore: "A Study of Alpha-Lobeline, Metrazol and Niketharnide in Experimental Anoxia."

Dr. Frank W. Hartman, Detroit: "Pathology in Anoxia," the chairman's address.

These six papers were discussed by Drs. F. A. D. Alexander, Albany, N. Y.; Robert L. Levy, New York; R. D. McClure, Detroit; Ernst Gellhorn, Chicago; Carl J. Wiggers, Cleveland; Harold Inman Gosline, Ossining, N. Y.; H. E. Himwich, Albany, N. Y.; Ralph M. Waters, Madison, Wis.; Frank W. Hartman, Detroit; Alvin G. Foord, Pasadena, Calif., and Nicholson J. Eastman, Baltimore.

Dr. L. W. Larson, Bismarck, N. D., delegate of the section to the House of Delegates, submitted his report, dealing principally with the expansion of state public health laboratory

work. Dr. Larson also reported on efforts being made to change the name of the section to "Section on Experimental Medicine" and offered the following resolution, which was unanimously adopted:

WHEREAS, The suggestion has been made to the Council on Scientific Assembly of the American Medical Association that the Section on Pathology and Physiology be combined with the Section on Pharmacology and Therapeutics to form a Section on Experimental Medicine; be it

Resolved, That the Section on Pathology and Physiology is opposed to such a change.

Drs. Frank W. Hartman, Detroit, and J. J. Moore, Chicago, were nominated for six year terms on the American Board of Pathology.

THURSDAY, JUNE 13—AFTERNOON

Dr. James F. Rinehart, San Francisco, read a paper on "Capillary Strength and Permeability in Rheumatoid Arthritis."

Dr. Max Cutler, Chicago, read a paper on "Cancer of the Larynx: Relation Between Gross Anatomy, Microscopic Structure and Radiosensitivity." Discussed by Drs. Chevalier L. Jackson, Philadelphia; Frank W. Konzelmann, Philadelphia, and Max Cutler, Chicago.

Dr. M. C. Winternitz, New Haven, Conn., read a paper on "Effects of Tissue Extracts on Normal and Nephrectomized Dogs." Discussed by Dr. Benjamin Jablons, New York.

Drs. Don C. Sutton and John Ashworth, Chicago, presented a paper on "Experimental Lesions of the Aorta Simulating Arteriosclerosis." Discussed by Drs. K. K. Jones, Chicago; J. P. Simonds, Chicago; M. C. Winternitz, New Haven, Conn., and Don C. Sutton, Chicago.

Dr. H. E. Robertson, Rochester, Minn., read a paper on "The Pathology of Brunner's Glands." Discussed by Dr. Carl J. Wiggers, Cleveland.

Drs. Ernest W. Page, Berkeley, Calif.; Henry S. Patton, Oakland, Calif., and Eric Ogden, Berkeley, Calif., presented a paper on "The Effect of Pregnancy on Experimental Hypertension." Discussed by Drs. Irvine H. Page, Indianapolis; Hans Selye, Montreal, Canada; Frank W. Hartman, Detroit; L. V. Dill, New York; T. R. Harrison, Nashville, Tenn., and Eric Ogden, Berkeley, Calif.

Dr. Hans Selye, Montreal, read a paper on "Compensatory Atrophy of Endocrine Glands." Discussed by Drs. Milton Steinberg, Chicago; J. P. Simonds, Chicago, and Hans Selye, Montreal.

A nominating committee was appointed, consisting of Drs. L. W. Larson, Bismarck, N. D.; H. C. Thornton, Indianapolis, and Alvin Foord, Pasadena, Calif.

FRIDAY, JUNE 14—AFTERNOON

The following officers were elected: chairman, Dr. Carl J. Wiggers, Cleveland; vice chairman, Dr. J. P. Simonds, Chicago; secretary, Dr. J. J. Moore, Chicago; delegate, Dr. L. W. Larson, Bismarck, N. D.; alternate, Dr. J. J. Moore, Chicago; executive committee: Drs. M. B. Visscher, Minneapolis; Frank W. Hartman, Detroit, and Carl J. Wiggers, Cleveland.

Drs. H. J. Corper, A. P. Damerow and Maurice L. Cohn, Denver, presented a paper on "Tuberculoprotein Desensitization and Tuberculosis." Discussed by Dr. Henry C. Sweany, Chicago.

Drs. G. B. Fauley, A. C. Ivy and A. J. Atkinson, Chicago, presented a paper on "The Use of Aluminum Phosphate in the Therapy of Peptic Ulcer." Discussed by Drs. Jesse L. Bollman, Rochester, Minn.; Hyman I. Goldstein, Camden, N. J.; I. H. Einsel, Cleveland, and A. C. Ivy, Chicago.

Drs. Elmer L. De Gowin and Robert C. Hardin, Iowa City, presented a paper on "Studies on Preserved Human Blood: VI. Reactions from Transfusion." Discussed by Drs. Alexander S. Wiener, Brooklyn; L. W. Diggs, Memphis, Tenn.; Hyman I. Goldstein, Camden, N. J.; Alvin G. Foord, Pasadena, Calif., and Elmer L. De Gowin, Iowa City.

Drs. Sidney O. Levinson, Frank E. Rubovits Jr. and Heinrich Necheles, Chicago, presented a paper on "Human Serum Transfusions." Discussed by Drs. Joseph A. Wagner, Bryn Mawr, Pa., and Sidney O. Levinson, Chicago.

Dr. Jesse L. Bollman, Rochester, Minn., read a paper on "The Influence of the Liver on the Utilization of Vitamin K." Discussed by Drs. Stephen J. Maddock, Boston; Jonathan Rhoads, Philadelphia, and Jesse L. Bollman, Rochester, Minn.

Drs. Henry C. Sweany and Charlotte Louise Clancy, Chicago, and Molly H. Radford, Santa Fe, N. M., presented a paper on "The Body Economy of Vitamin C in Health and Disease with Special Studies in Tuberculosis."

Dr. Bernhard Steinberg, Toledo, Ohio, read a paper on "Peritoneal Exudate: A Guide for the Diagnosis and Prognosis of Peritoneal Conditions." Discussed by Drs. Frank L. Meleney, New York, and Bernhard Steinberg, Toledo, Ohio.

SECTION ON NERVOUS AND MENTAL DISEASES

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:25 by the chairman, Dr. Paul C. Bucy, Chicago.

Drs. William F. Petersen, Chicago, and Hans H. Reese, Madison, Wis., presented a paper on "Psychotic and Somatic Interrelations." Discussed by Lloyd H. Ziegler, Wauwatosa, Wis.; Irving J. Sands, Brooklyn, and Hans H. Reese, Madison, Wis.

Dr. A. R. Vonderahe, Cincinnati, read a paper on "Sequelae of Severe Disease of the Abdominal Viscera with Special Reference to Psychoneurosis and Imbalance of the Autonomic Nervous System." Discussed by Drs. Leo Alexander, Boston; Robert G. Green, Minneapolis; Norman Jolliffe, New York; John F. Fulton, New Haven, Conn., and A. R. Vonderahe, Cincinnati.

Dr. Samuel D. Ingham, Los Angeles, read a paper on "Instinctive Motivations of Suicide." Discussed by Drs. A. A. Brill, New York; Titus H. Harris, Galveston, Texas, and Samuel D. Ingham, Los Angeles.

Drs. Herbert Jasper, John Kershman and A. R. Elvidge, Montreal, presented a paper on "Electro-Encephalographic Studies of Head Injury." Discussed by Drs. Tracy J. Putnam, New York; Robert S. Schwab, Boston; Max H. Weinberg, Pittsburgh, and John Kershman, Montreal.

Dr. Russell N. DeJong, Ann Arbor, Mich., read a paper on "Acute Ascending Paralysis with Clinical and Pathologic Report on Cases with Fatal Termination."

Drs. Paul H. Garvey, Nathaniel Jones and Stafford L. Warren, Rochester, N. Y., presented a paper on "Polyradiculoneuritis (Guillain-Barré Syndrome)."

These two papers were discussed by Drs. Louis Casamajor, New York; Peter Bassoe, Chicago; A. M. Ornsteen, Philadelphia; Frederick P. Moersch, Rochester, Minn.; A. E. Bennett, Omaha; Norman Jolliffe, New York; Paul C. Bucy, Chicago; Irving J. Sands, Brooklyn; A. M. Rabiner, Brooklyn; Ralph Hayward, Toronto; Russell N. DeJong, Ann Arbor, Mich., and Paul H. Garvey, Rochester, N. Y.

THURSDAY, JUNE 13—MORNING

The following officers were elected: chairman, Tom B. Throckmorton, Des Moines, Iowa; vice chairman, Titus H. Harris, Galveston, Texas; secretary, Johannes M. Nielsen, Los Angeles; executive committee: Francis C. Grant, Philadelphia; Paul C. Bucy, Chicago, and Tom B. Throckmorton, Des Moines, Iowa; delegate, Henry R. Viets, Boston; alternate, R. P. Mackay, Chicago; representative to Scientific Exhibit, Frederick P. Moersch, Rochester, Minn.; representative on American Board of Psychiatry and Neurology, Lloyd H. Ziegler, Wauwatosa, Wis.; representative on American Board of Neurosurgery, Paul C. Bucy, Chicago.

Dr. Walter Freeman, Washington, D. C., gave a report from the American Board of Psychiatry and Neurology, which was accepted.

Dr. Paul C. Bucy, Chicago, gave a report from the American Board of Neurosurgery, which was accepted.

The section approved for transmittal to the House of Delegates a resolution recommending the establishment in the United States Public Health Service of an institute for the study of mental and nervous diseases.

The section approved for transmittal to the House of Delegates a resolution approving the plan known as the Pennsylvania plan applicable to medicolegal cases in the handling of criminals.

Dr. Frederick P. Moersch, Rochester, Minn., read a paper on "Primary and Secondary Melanoma of the Central Nervous System." Discussed by Drs. S. Bernard Wortis, New York; Peter Bassoe, Chicago; Hans H. Reese, Madison, Wis., and Frederick P. Moersch, Rochester, Minn.

Drs. Bernard J. Alpers and F. H. Lewy, Philadelphia, presented a paper on "The Nervous System in Carbon Disulfide Poisoning in Animals and Man." Discussed by Drs. S. T. Gordy, Philadelphia; Armando Ferraro, New York; Philip Drinker, Cambridge, Mass.; Noble R. Chambers, Syracuse, N. Y.; Bernard J. Alpers, Philadelphia, and F. H. Lewy, Philadelphia.

Dr. Paul C. Bucy, Chicago, read the chairman's address, entitled "Surgical Neurology and Biology."

Drs. Louis J. Karnosh, Cleveland, and Roger F. Scherb, Camarillo, Calif., presented a paper on "The Significance of Trophic Lesions in the Trigeminal Area." Discussed by Drs. Max Minor Peet, Ann Arbor, Mich.; A. Earl Walker, Chicago, and Byron Stookey, New York.

Drs. Orthello R. Langworthy and Frederick H. Hesser, Baltimore, presented a paper on "The Control of Smooth Muscle by the Nervous System." Discussed by Drs. J. W. Watts, Washington, D. C.; Lloyd G. Lewis, Baltimore, and John F. Fulton, New Haven, Conn.

Drs. Eric Oldberg and W. A. Gustafson, Chicago, presented a paper on "The Neurologic Significance of Platybasia." Discussed by Drs. Tracy J. Putnam, New York; Leo M. Davidoff, Brooklyn, and Eric Oldberg, Chicago.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Ophthalmology. The proceedings are reported in the minutes of that section.

SECTION ON DERMATOLOGY AND SYPHILOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9:15 by the chairman, Dr. John G. Downing, Boston.

Dr. John G. Downing read the chairman's address, entitled "Dermatitis."

Drs. James W. Jordan and Earl D. Osborne, Buffalo, presented a paper on "Dermatitis of the Hands in Housewives: Role of Soaps in Its Etiology and Methods for Its Prevention." Discussed by Drs. Joseph V. Klauder, Philadelphia; Marion B. Sulzberger, New York; Herman Goodman, New York; Joseph Muller, Worcester, Mass.; Adolph Rostenberg Jr., Washington, D. C.; Howard J. Parkhurst, Toledo, Ohio; Donald M. Pillsbury, Philadelphia, and James W. Jordan, Buffalo.

Dr. John H. Stokes, Philadelphia, read a paper on "The Personality Factor in the Psychoneurogenous Reactions of the Skin." Discussed by Drs. Harry C. Solomon, Boston; Eugene T. Bernstein, New York; Henry D. Niles, New York; S. William Becker, Chicago; Samuel Ayres Jr., Los Angeles; Joseph V. Klauder, Philadelphia; Marion B. Sulzberger, New York, and John H. Stokes, Philadelphia.

Dr. Lawrence C. Goldberg, Cincinnati, read a paper on "Histaminase (Torantil) in the Treatment of Allergic Dermatoses." Discussed by Drs. G. Marshall Crawford, Boston; Ashton L. Welsh, Cincinnati; Herman Goodman, New York; Herman Sharlit, New York, and Lawrence C. Goldberg, Cincinnati.

Dr. M. H. Goodman, Baltimore, read a paper on "Dermatitis Herpetiformis: Influence of Age Factors and a Study of Pathologic Data with Special Reference to Eosinophils." Discussed by Drs. Isadore Rosen, New York; Jacob H. Swartz, Boston; Henry D. Niles, New York; Theodore Cornbleet, Chicago, and M. H. Goodman, Baltimore.

Dr. Stephen Epstein, Marshfield, Wis., read a paper on "Staphylococcic Impetigo Contagiosa." Discussed by Drs. Marion B. Sulzberger, New York; Richard S. Weiss, St. Louis, and Stephen Epstein, Marshfield, Wis.

Dr. John F. Madden, St. Paul, read a paper on "Treatment of Psoriasis." Discussed (at the Thursday session) by Drs. Donald M. Pillsbury, Philadelphia; Joseph V. Klauder, Philadelphia, and John F. Madden, St. Paul.

THURSDAY, JUNE 13—MORNING

The chairman asked that any member having business to go before the House of Delegates should present it on the floor during this business session.

The chairman then introduced Dr. Jose J. Puento, Buenos Aires.

It was moved by Dr. Harold N. Cole, Cleveland, seconded by Dr. Paul A. O'Leary, Rochester, Minn., and carried, that Dr. Puento be given the courtesy of the floor.

Dr. Hamilton Montgomery, Rochester, Minn., representative to the Scientific Exhibit from the section, read his prepared report. (Paper No. 1.)

The Chairman appointed the following auditing committee to audit Dr. Montgomery's financial statement: Drs. William P. Boardman, Boston; W. M. Sams, Miami, Fla., and H. F. Anderson, Washington, D. C.

Dr. Paul A. O'Leary, Rochester, Minn., turned in the financial report on the International Congress of Dermatology and Syphilology. He stated that the expenditures had been about $2,000 and that there was a balance of a few hundred dollars on hand which they did not know what to do with but were appreciative of the financial efforts of those who contributed to the fund and were sorry that the balance had not been put to better use.

Dr. C. Guy Lane, Boston, gave his report of the American Board of Dermatology and Syphilology.

Reporting for the Committee on Industrial Dermatoses, Dr. C. Guy Lane, Boston, stated: The committee has agreed on a definition and is working out the criteria of occupational dermatoses, with a view of submitting these criteria to the Council on Industrial Health of the American Medical Association. A list of primary irritants is also being prepared by the committee, and there is also a study of the so-called eczematous substances. There has been, and there will be again today, a discussion with members of the Council on Industrial Health on the matter of setting up a central clearing house, perhaps, for a further study of occupational dermatoses, possibly with reference to the collection of reports with reference to the application of criteria regarding reportability of data, of reference material, and so on, and a further report on these items will be rendered next year.

It was moved by Dr. C. Guy Lane, Boston, seconded by Dr. Francis P. McCarthy, Boston, and carried, that in view of the fact that a committee was appointed at the American Dermatological Association for a further study of contact dermatoses, a similar committee of three be appointed by the chairman to cooperate with the committee from the American Dermatological Association, and also probably a committee from the investigative society, to continue to cooperate in such investigations.

The auditing committee appointed to audit the report on the Scientific Exhibit reported that it approved the report.

Dr. Francis P. McCarthy, Boston, read a paper on "A Clinical and Pathologic Study of Oral Disease, Based on 2,300 Consecutive Cases." Discussed by Drs. Frank J. Eichenlaub, Washington, D. C.; Samuel Ayers Jr., Los Angeles, and Francis P. McCarthy, Boston.

Drs. William H. Guy, Bernhard A. Goldmann, George P. Gannon and Jacob Slone, Pittsburgh, presented a paper on "Acetylglyco-Arsenobenzene in the Treatment of Syphilis." Discussed by Drs. Harry M. Robinson, Baltimore; Joseph Earle Moore, Baltimore, and William H. Guy, Pittsburgh.

Drs. Harold N. Cole, Gerard A. DeOreo, James R. Driver and Herbert H. Johnson Jr., Cleveland, and Walter F. Schwartz, Pasadena, Calif., presented a paper on "The Use of Bismuth Injections to Control the Course of Therapeutic Malaria." Discussed by Drs. Paul A. O'Leary, Rochester, Minn., and Harold N. Cole, Cleveland.

Dr. Edmund N. Walsh, Chicago, read a paper on "The Use of Bismuth in Syphilotherapy." Discussed by Drs. Donald M. Pillsbury, Philadelphia, and S. William Becker, Chicago.

Dr. Albert Strickler, Philadelphia, read a paper on "The Aschheim-Zondek Test in Cutaneous and Mammary Malignant Growths." Discussed by Drs. Milton H. Cohen, York, Pa., and Albert Strickler, Philadelphia.

Dr. Louie H. Winer, Minneapolis, read a paper on "Pseudo-Epitheliomatous Hyperplasia." Discussed by Drs. Hamilton Montgomery, Rochester, Minn.; Fred D. Weidman, Philadelphia; J. Frank Fraser, New York, and Louie H. Winer, Minneapolis.

FRIDAY, JUNE 14—MORNING

The chairman appointed the following Committee on Contact Dermatoses: Dr. Earl D. Osborne, Buffalo; Dr. Louis A. Brunsting, Rochester, Minn., and Dr. Edward A. Oliver, Chicago.

The following officers were elected: chairman, Dr. Joseph Gardner Hopkins, New York; vice chairman, Dr. Edward A. Oliver, Chicago; secretary, Dr. C. F. Lehmann, San Antonio, Texas; representative to the Scientific Exhibit, Hamilton Montgomery, Rochester, Minn.; delegate, Dr. Clyde L. Cummer, Cleveland; alternate, Dr. Harold N. Cole, Cleveland; representative to fill the vacancy on the American Board of Dermatology, Dr. C. Guy Lane, Boston.

Dr. Harold N. Cole, Cleveland, stated that the Committee on Scientific Exhibit was to be congratulated on the work it has done, as there have been two honorable mentions and two certificates of merit in this section.

Dr. Herbert L. Traenkle, Buffalo, read a paper on "The Relationship Between Epithelioma Adenoides Cysticum, Tricho-Epithelioma and Basal Cell Cancer as Illustrated by Histologic Studies of Multiple Benign Cystic Epithelioma."

Dr. Hyman J. Goldman, St. Louis, read a paper on "Multiple Benign Cystic Epithelioma: Report of Ten Cases in One Family."

These two papers were discussed by Drs. Fred D. Weidman, Philadelphia; Hamilton Montgomery, Rochester, Minn.; Herman Goodman, New York; David Bloom, New York; Richard L. Sutton Jr., Kansas City, Mo.; Herbert L. Traenkle, Buffalo, and Hyman J. Goldman, St. Louis.

Drs. C. W. Emmons, Washington, D. C., and W. Howard Hailey and Hugh Hailey, Atlanta, Ga., presented a paper on "Chromoblastomycosis: Report of the Sixth Case from Continental United States." Discussed by Drs. Joseph Gardner Hopkins, New York; W. M. Sams, Miami, Fla.; Fred D. Weidman, Philadelphia; Morris Moore, St. Louis (by motion extending the privilege of the floor to Dr. Moore), and Hugh Hailey, Atlanta, Ga.

Dr. Leslie M. Smith, El Paso, Texas, read a paper on "Blastomycosis and the Blastomycosis-like Infections." Discussed by Drs. George M. Lewis, New York, and Leslie M. Smith, El Paso, Texas.

Dr. Frederic T. Becker, Duluth, Minn., read a paper on "Milkers' Nodules." Discussed by Drs. M. E. Obermayer, Chicago; C. Guy Lane, Boston, and Frederic T. Becker, Duluth, Minn.

Dr. E. E. Barksdale, Danville, Va., read a paper on "Cutaneous Manifestations from Tobacco with Special Reference to Arsenical Exfoliative Dermatitis." Discussed by Drs. Dudley C. Smith, Charlottesville, Va.; Harry M. Robinson, Baltimore; Marion B. Sulzberger, New York; Herman Sharlit, New York, and E. E. Barksdale, Danville, Va.

Drs. Charles P. Bondurant, Oklahoma City, read a paper on "Adrenal Cortex Extract in the Treatment of Bromide Eruption and Bromide Intoxication." Discussed by Drs. Eugene F. Traub, New York; E. W. Abramowitz, New York; Richard L. Sutton Jr., Kansas City, Mo., and Charles P. Bondurant, Oklahoma City.

The retiring chairman introduced the incoming chairman, Dr. Joseph Gardner Hopkins, New York.

Dr. C. Guy Lane, Boston, moved a vote of thanks to the New York committee and all who were engaged in making this meeting a very successful one, for the entertainment, excellent quarters and luncheon on Thursday. The motion was seconded by Dr. Paul A. O'Leary, Rochester, Minn., and carried.

SECTION ON PREVENTIVE AND INDUSTRIAL MEDICINE AND PUBLIC HEALTH

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the vice chairman, Dr. Clarence D. Selby, Detroit.

Dr. Edgar Mayer, New York, read a paper on "The Clinical Evaluation of Disability in Industrial Pulmonary Diseases." Discussed by Drs. J. Burns Amberson Jr., New York, and Edgar Mayer, New York.

Drs. Robert G. Bloch, William B. Tucker and J. Edmond Bryant, Chicago, presented a paper on "Roentgenologic Group Examinations for Pulmonary Tuberculosis in Negroes in Chicago: A Preliminary Report." Discussed by Drs. Max Pinner, New York; H. R. Edwards, New York; Arthur B. Robins, New York; Haven Emerson, New York, and Robert B. Bloch, Chicago.

Drs. Leonard Greenburg and Adelaide R. Smith, New York, and William T. Siegal, Albany, N. Y., presented a paper on "Medical Aspects of Four Years of Compensation for Silicosis in New York State."

Drs. Arthur M. Master and Simon Dack, New York, presented a paper on "Rehabilitation Following Coronary Occlusion." Discussed by Drs. Harry E. Ungerleider, New York; Cary Eggleston, New York, and Clifford Kuh, New Haven, Conn.

Dr. H. M. F. Behneman, San Francisco, read a paper on "Should Coronary Disease and Hypertension Be a Cause for Rejection in Industry?" Discussed by Drs. Nelson D. Morris, Toledo, Ohio; Robert T. Legge, Berkeley, Calif.; C. W. Roberts, Atlanta, Ga.; E. J. Stieglitz, Washington, D. C.; Arthur M. Master, New York, and H. M. F. Behneman, San Francisco.

THURSDAY, JUNE 13—AFTERNOON

Dr. Harold S. Diehl, Minneapolis, read the chairman's address, entitled "Medical Careers in Public Health."

Homer N. Calver, New York, read a paper on "Health Information Please." Discussed by Drs. Harrison S. Martland, Newark, N. J.; Millard Knowlton, Hartford, Conn., and Homer N. Calver, New York.

Dr. Charles-Francis Long, Philadelphia, read a paper on "A Program for Industrial Health in State and County Medical Societies." Discussed by Drs. Albert S. Gra Hartford, Conn., and Charles-Francis Long, Philadelphia.

Dr. Thomas L. Shipman, Lynn, Mass., read a paper on "Opportunities for Physicians in Industry." Discussed by Dr. M. N. Newquist, New York.

Dr. A. Grant Fleming, Montreal, Canada, read a paper on "Preventive Medicine in General Practice." Discussed by Drs. Reginald Fitz, Boston; Haven Emerson, New York; Clifford Kuh, New Haven, Conn., and A. Grant Fleming, Montreal, Canada.

Dr. M. E. Barnes, Iowa City, read a paper on "Applied Epidemiology in the General Hospital." Discussed by Drs. W. G. Smillie, New York, and Leopold Brahdy, New York.

FRIDAY, JUNE 14—AFTERNOON

Drs. John R. Paul and James D. Trask, New Haven, Conn., presented a paper on "Poliomyelitis Virus in Human Stools and in Sewage."

Drs. Howard A. Howe and David Bodian, Baltimore, presented a paper on "The Portal of Entry in Poliomyelitis."

Dr. W. Lloyd Aycock, Boston, read a paper on "The Frequency of Poliomyelitis in Pregnancy."

These three papers were discussed by Drs. James P. Leake, Washington, D. C.; T. M. Rivers, New York; Harold L. Amoss, Greenwich, Conn.; James D. Trask, New Haven, Conn., and Howard A. Howe, Baltimore.

The following officers were elected: chairman, Dr. Clarence D. Selby, Detroit; vice chairman, Dr. Huntington Williams, Baltimore; secretary, Dr. W. A. Sawyer, Rochester, N. Y.; executive committee: Dr. I. C. Riggin, Richmond, Va.; Dr. Harold S. Diehl, Minneapolis, and Dr. Clarence D. Selby, Detroit; chairman, Committee on Section Exhibit, Dr. P. A. Davis, Akron, Ohio.

Dr. Lowell S. Selling, Detroit, read a paper on "The Mental Hygiene Aspect of the Traffic Accident." Discussed by Dr. Daniel Blain, New York.

Drs. Murray B. Ferderber and F. C. Houghten, Pittsburgh, presented a paper on "Effective Temperature Scale: A Measure of Human Comfort in Environmental Temperature." Discussed by Dr. W. J. McConnell, New York.

SECTION ON UROLOGY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2:05 by the chairman, Dr. Frederic E. B. Foley, St. Paul.

Drs. William F. Braasch, Waltman Walters and Howard J. Hammer, Rochester, Minn., presented a paper on "Hypertension and the Surgical Kidney."

Drs. E. Granville Crabtree and Nathan Chaset, Boston, presented a paper on "A Combined Clinical and Clinicopathologic Study of 150 Nephrectomized Patients in Respect to Vascular Nephritis and Hypertension."

These two papers were discussed by Drs. Stanford W. Mulholland, Philadelphia; Roy J. Holmes, Miami, Fla.; Earl E. Ewert, Boston; James F. McCahey, Philadelphia; George W. Fish, New York; William F. Braasch, Rochester, Minn., and Nathan Chaset, Boston.

Drs. Budd C. Corbus and Budd C. Corbus Jr., Chicago, presented a paper on "The Cutaneous Diagnosis of Gonococcic Infections Illustrated with Kodachrome Transparencies: A Further Report." Discussed by Drs. Michael Wishengrad, New York; John H. Morrissey, New York, and Budd C. Corbus, Chicago.

Dr. Russell D. Herrold, Chicago, read a paper on "Chemotherapy in the Treatment of Gonorrhea."

Drs. Edwin P. Alyea, Durham, N. C., read a paper on "The Present Status of Chemotherapy in Nonspecific Infections of the Urinary Tract."

Drs. Grayson L. Carroll, Louis C. Kappel and Bransford Lewis, St. Louis, presented a paper on "Therapy with the Thiazole Compounds of Sulfanilamide."

These three papers were discussed by Drs. Charles A. W. Uhle, Philadelphia; V. Rogers Deakin, St. Louis; P. S. Pelouze, Philadelphia; W. Ray Jones, Seattle; Reed M. Nesbit, Ann Arbor, Mich., and Russell D. Herrold, Chicago.

THURSDAY, JUNE 13—AFTERNOON

Dr. Frederic E. B. Foley, St. Paul, read the chairman's address, entitled "Surgical Correction of Horseshoe Kidney."

Dr. Hugh H. Young, Baltimore, read a paper on "Pathology and Surgical Treatment of Vesical Neck Obstruction in Women." Discussed by Drs. Henry Dawson Furniss, New York; Alf H. Gundersen, La Crosse, Wis.; Edward N. Cook, Rochester, Minn.; T. Leon Howard, Denver, and Hugh H. Young, Baltimore.

Drs. H. M. Stang and A. J. Hertzog, Eau Claire, Wis., presented a paper on "Primary Carcinoma of the Ureter: A Report of Four Cases."

Drs. Edward N. Cook and Virgil S. Counseller, Rochester, Minn., presented a paper on "Primary Epithelioma of the Ureter."

These two papers were discussed by Drs. Paul A. Ferrier, Pasadena, Calif.; Monroe E. Greenberger, New York; Hugh H. Young, Baltimore; T. Leon Howard, Denver, and Virgil S. Counseller, Rochester, Minn.

Dr. James C. Sargent, Milwaukee, read a paper on "Injury of the Kidneys with Special Reference to Early and Accurate Diagnosis Through Pyelography." Discussed by Drs. Roy B. Henline, New York; George F. Cahill, New York; William Calhoun Stirling, Washington, D. C.; Vincent J. O'Conor, Chicago, and James C. Sargent, Milwaukee.

Dr. Edwin Davis, Omaha, read a paper on "Technic and Results in Perineal Prostatectomy" and showed a motion picture of the operation. Discussed by Drs. Oswald Swinney Lowsley, New York; Hugh H. Young, Baltimore, and Edwin Davis, Omaha.

The chairman announced that in the elections for the coming year three urologists had been elected to offices in the American Medical Association: Dr. Herman L. Kretschmer, Chicago, treasurer; Dr. William F. Braasch, Rochester, Minn., to the Board of Trustees, and Dr. Parke G. Smith, Cincinnati, vice president.

FRIDAY, JUNE 14—AFTERNOON

The following officers were elected: chairman, Dr. Meredith F. Campbell, New York; vice chairman, Dr. L. F. Huffman, Cleveland; secretary, Dr. Vincent J. O'Conor, Chicago; delegate, Dr. Hermon C. Bumpus Jr., Pasadena, Calif., and alternate, Dr. George C. Prather, Boston.

The chairman read the following recommendation from the executive committee: In the past there has been no recorded stipulation or approved precedent covering the nominations of our representatives for election by the American Board of Urology, Inc., to its membership. The nomination of none of our present representatives on the board has had approval by vote of the section.

Your executive committee recommends that in the future its nominations for election of representatives by the American Board of Urology, Inc., to its membership be submitted to the members of the section for approval by vote.

On motion by Dr. Grayson L. Carroll, St. Louis, seconded by Dr. T. Leon Howard, Denver, the recommendation was adopted.

The chairman asked the secretary to present nominations of the executive committee for membership on the Board of Urology, stating that there were two places to be filled.

The secretary stated that he would like to acquaint the section with the present status of the American Board of Urology, Inc., constitution, which had been changed during the past year as regards election of members of the board, and further stated: I have been confronted as secretary with a situation where there has been considerable confusion as to what constituted a legal and acceptable nomination of this section to the board. After an extensive research, I found no recorded procedure either in the previous minutes of the section or definite data from the American board itself. For this reason the executive committee felt that, in order to make the selection of our men to the American board without question as far as the executive committee is concerned, the recommendation which the chairman just read should be made. The executive committee feels that the selection of these men should be a part of the regular procedure of this section and that every one should have a voice in the matter, and in that way every one will feel that he is having a part in selecting representative men to represent this section on the board.

Prior to this year the executive committee has selected one man, whose name has been sent to the American board. During the past year the American board has changed its method of selecting from this section and others.

The secretary then read from correspondence from the American Board of Urology, Inc., regarding the method of selecting members, as follows:

> Each nominating society may submit to the board of trustees the names of not lesss than three of their eligible member physicians as its nominees in the alternative, for each successor membership to which a nominee of such nominating society shall be eligible for election, but if any such nominating society shall fail so to submit the names of three or more such nominees not later than ten days prior to the meeting of the members, annual or special, at which the election of such successor member is scheduled to take place, or if no such nominee shall receive sufficient votes to elect him to membership, then, and in either such event, the board of trustees, by a majority vote, may designate any eligible member of such nominating society as the nominee of such nominating society for election to such successor membership of this corporation.

The section then voted to recommend the following nominations for the American Board of Urology, Inc.:

For a four year term: Dr. Clarence G. Bandler, New York; Dr. Frank Hinman, San Francisco; Dr. Miley B. Wesson, San Francisco.

For a five year term: Dr. Alfred I. Folsom, Dallas, Texas; Dr. Albert E. Goldstein, Baltimore; Dr. Thomas D. Moore, Memphis, Tenn.

Dr. Henry A. R. Kreutzmann, San Francisco, read a paper on "Sterility in the Male: Diagnosis and Treatment."

Drs. Samuel R. Meaker and Samuel N. Vose, Boston, presented a paper on "The Nature of Human Infertility."

Dr. Charles W. Charny, Philadelphia, read a paper on "Testicular Biopsy: Its Value in Male Sterility."

Dr. Francis R. Hagner, Washington, D. C., read a paper on "The Operative Treatment of Sterility in the Male: Further Report, with Table of Results in Eighty-Five Cases."

These four papers were discussed by Drs. Robert S. Hotchkiss, New York; Max Huhner, New York; Henry Sangree, Philadelphia; W. W. Williams, Springfield, Mass.; Henry A. R. Kreutzmann, San Francisco; Charles W. Charny, Philadelphia, and Francis R. Hagner, Washington, D. C.

Drs. Bernard Strauss and Gerson R. Biskind, San Francisco, presented a paper on "The Implantation of Pellets of Methyl Testosterone in the Treatment of Eunuchoidism."

Dr. Walter M. Kearns, Milwaukee, read a paper on "The Oral Administration of Methyl Testosterone in Testicular Deficiency."

These two papers were discussed by Drs. Norris J. Heckel, Chicago; Samuel A. Vest Jr., Charlottesville, Va.; William P. Herbst Jr., Washington, D. C.; Charles W. Dunn, Philadelphia; Bernard Strauss, San Francisco, and Walter M. Kearns, Milwaukee.

The secretary expressed the thanks and appreciation of the section to the New York committee, Dr. Clarence G. Bandler, Dr. Roy B. Henline, Dr. Francis N. Kimball and Dr. Meredith F. Campbell, for their splendid cooperation in making the meeting a success.

SECTION ON ORTHOPEDIC SURGERY

WEDNESDAY, JUNE 12—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Robert V. Funsten, Charlottesville, Va.

Drs. William B. Carrell Jr. and Brandon Carrell, Dallas, Texas, presented a paper on "Fractures of the Neck of the Femur in Children." Discussed by Drs. Mark H. Rogers, Boston; James A. Dickson, Cleveland; Francis M. McKeever, Los Angeles, and William B. Carrell Jr., Dallas, Texas.

Dr. James E. M. Thomson, Lincoln, Neb., read a paper on "A Program for the Treatment of Compound Fractures." Discussed by Drs. Robert W. Johnson Jr., Baltimore; Donald E. McKenna, Brooklyn; Myron O. Henry, Minneapolis; Harold R. Bohlman, Baltimore, and James E. M. Thomson, Lincoln, Neb.

Drs. G. Mosser Taylor and Alonzo J. Neufeld, Los Angeles, presented a paper on "External or Internal Fixation for Intertrochanteric Fractures." Discussed by Drs. Frank M. Hand, Washington, D. C.; Armitage Whitman, New York; Abraham M. Rechtman, Philadelphia, and G. Mosser Taylor, Los Angeles.

A nominating committee was appointed, consisting of Drs. James E. M. Thomson, Lincoln, Neb., chairman; Ralph Ghormley, Rochester, Minn.; W. Barnett Owen, Louisville, Ky., and Philip Lewin, Chicago.

Dr. Jesse T. Nicholson, Philadelphia, read a paper on "Spontaneous Reduction of Cervical Spine Dislocation in Children." Discussed by Drs. William H. Von Lackum, New York; Barbara B. Stimson, New York, and Jesse T. Nicholson, Philadelphia.

Dr. Charles R. Rountree, Oklahoma City, read a paper on "Diaphysectomy for Chronic Osteomyelitis of the Fibula." Discussed by Drs. John R. Cobb, New York, and Charles R. Rountree, Oklahoma City.

Dr. Howard A. Swart, Charleston, W. Va., read a paper on "The Use of Double Wire Traction in the Treatment of Fractures of the Shaft of the Femur." Discussed by Drs. George W. Van Gorder, Boston; Clay Ray Murray, New York; John P. Stump, New York, and Howard A. Swart, Charleston, W. Va.

THURSDAY, JUNE 13—AFTERNOON

Dr. Hira E. Branch, Detroit, read a paper on "Progressive Pseudohypertrophic Muscular Dystrophy: A New Regimen of Treatment." Discussed by Drs. Joseph B. L'Episcopo, Brooklyn; Joseph A. Freiberg, Cincinnati; Ralph K. Ghormley, Rochester, Minn., and Hira E. Branch, Detroit.

The following officers were elected: chairman, J. Albert Key, St. Louis; vice chairman, James A. Dickson, Cleveland; secretary, Guy A. Caldwell, New Orleans; executive committee: Oscar L. Miller, Charlotte, N. C.; Robert V. Funston, Charlottesville, Va., and J. Albert Key, St. Louis; delegate, James Archer O'Reilly, St. Louis; alternate, William B. Carrell Jr., Dallas, Texas; nominees to the American Board of Orthopedic Surgery, James S. Speed, Memphis, Tenn., and Frank R. Ober, Boston.

Dr. Gilbert E. Haggart, Boston, read a paper on "Early Operation (Spine Fusion) in Unstable Lumbosacral Joints." Discussed by Drs. Allen F. Voshell, Baltimore; Frederick A. Jostes, St. Louis, and Gilbert E. Haggart, Boston.

Dr. Robert V. Funsten, Charlottesville, Va., read the chairman's address, entitled "Problems in Fractures of the Lower Third of the Femur."

Dr. Frank G. Murphy, Chicago, read a paper on "Surgical Closure of Osseous Tuberculous Abscesses." Discussed by Drs. Robert J. Cook, New Haven, Conn.; John R. Cobb, New York, and Frank G. Murphy, Chicago.

Dr. Harold R. Bohlman, Baltimore, read a paper on "An Improved Technic for Removal of the Semilunar Cartilage and the Postoperative Treatment." Discussed by Drs. Alan DeForest Smith, New York; Philip Lewin, Chicago, and Harold R. Bohlman, Baltimore.

Dr. James Archer O'Reilly, St. Louis, delegates to the House, made a report on the session of the House of Delegates, which was accepted.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Surgery, General and Abdominal. The proceedings are reported in the minutes of that section.

SECTION ON GASTRO-ENTEROLOGY AND PROCTOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman, Dr. A. H. Aaron, Buffalo.

Drs. Abraham J. Gitlitz, Englewood, N. J., and Henry H. Lerner, Boston, presented a paper on "Interpretation of Gastroscopic Observations in Terms of Mucosal Changes: Histologic Study."

Dr. Chester M. Jones, Boston, read a paper on "Clinical and Therapeutic Implications of Gastritis."

These two papers were discussed by Drs. Burrill B. Crohn, New York; Herman J. Moersch, Rochester, Minn.; Alfred S. White, San Francisco; Allan L. Cohn, San Francisco; Julian M. Ruffin, Durham, N. C.; William A. Swalm, Philadelphia; Lester M. Morrison, Philadelphia; Abraham J. Gitlitz, Englewood, N. J., and Chester M. Jones, Boston.

Dr. Frank C. Val Dez, Chicago, read a paper on "The Night Secretion of Hydrochloric Acid in the Stomach."

Drs. Herbert C. Breuhaus and James B. Eyerly, Chicago, presented a paper on "Antacids: Their Reaction by Titration and Within the Human Stomach."

These two papers were discussed by Drs. Moses Einhorn, New York; Harry Gauss, Denver; David J. Sandweiss, Detroit; Asher Winkelstein, New York; V. C. Rowland, Cleveland; Isidor Greenwald, New York; Leo L. Hardt, Chicago; John M. Blackford, Seattle; Walter L. Palmer, Chicago; Herbert C. Breuhaus, Chicago, and Frank C. Val Dez, Chicago.

Drs. Russell S. Boles, Helena E. Riggs, and John O. Griffiths, Philadelphia, presented a paper on "Neurogenic Factors in Production of Peptic Ulcer."

Drs. Leon Schiff, Richard J. Stevens and Harold K. Moss, Cincinnati, presented a paper on "The Prognostic Significance of the Blood Urea Nitrogen Following Hematemesis or Melena."

Drs. Clarence E. Bird, Providence, R. I., Margaret A. Limper, Louisville, Ky., and Jacob M. Mayer, Mayfield, Ky., presented a paper on "Surgery in Peptic Ulcer of Infants and Children."

Dr. John M. Blackford, Seattle, read a paper on "Fatal Hemorrhage from Peptic Ulcer."

These four papers were discussed by Drs. Walter L. Palmer, Chicago; Sidney Leibowitz, New York; Julius Chasnoff, New York; Irving Gray, Brooklyn; Burrill B. Crohn, New York; Arthur W. Allen, Boston; Andrew B. Rivers, Rochester, Minn.; Hyman I. Goldstein, Camden, N. J.; Anthony Bassler, New

York; Henry N. Harkins, Detroit; Horace W. Soper, St. Louis; Leon Bloch, Chicago; Harry L. Segal, Rochester, N. Y.; I. R. Jankelson, Boston; Frederick W. Mulsow, Cedar Rapids, Iowa; Russell S. Boles, Philadelphia; Helena E. Riggs, Philadelphia; Leon Schiff, Cincinnati; Clarence E. Bird, Providence, R. I., and John M. Blackford, Seattle.

THURSDAY, JUNE 13—MORNING

Drs. Donovan C. Browne and George Gordon McHardy, New Orleans, presented a paper on "Primary Jejunal Pathology." Discussed by Drs. David Adlersberg, New York; Maurice Feldman, Baltimore, and Donovan C. Browne, New Orleans.

Drs. E. G. Wakefield and N. T. Friedell, Rochester, Minn., presented a paper on "The Structural Significance of the Ileocecal Valve." Discussed by Drs. Ernest H. Gaither, Baltimore; Jacob M. Ravid, New York, and E. G. Wakefield, Rochester, Minn.

Drs. Maurice M. Rothman and Harry J. Epstein, Philadelphia, presented a paper on "A Clinical Entity Associated with the So-Called Nonpathogenic Ameba." Discussed by Drs. Asher Winkelstein, New York; Horace W. Soper, St. Louis; Palmer Dysart, Phoenix, Ariz.; Moses Paulson, Baltimore; Anthony Bassler, New York, and Maurice M. Rothman, Philadelphia.

Drs. Jacob Gershon-Cohen and Harry Shay, Philadelphia, presented a paper on "Carcinoma of the Colon: Early Diagnosis with Double Contrast Enema." Discussed by Drs. E. C. Koenig, Buffalo; Louis J. Hirschman, Detroit; B. R. Kirklin, Rochester, Minn., and Jacob Gershon-Cohen, Philadelphia.

Drs. Leo L. Hardt and Seymour J. Cohen, Chicago, presented a paper on "Gastrointestinal Complications in Pulmonary Tuberculosis." Discussed by Drs. Joseph Felsen, New York; Julius Friedenwald, Baltimore; Russell S. Boles, Philadelphia; Emil Granet, New York; Clement L. Martin, Chicago; Henry L. Bockus, Philadelphia, and Leo L. Hardt, Chicago.

Dr. Sara M. Jordan, Boston, read a paper on "End Results in Radical Gastrointestinal Surgery as Seen by the Gastro-Enterologist." Discussed by Drs. John G. Mateer, Detroit; Henry L. Bockus, Philadelphia; A. H. Aaron, Buffalo, and Sara M. Jordan, Boston.

Dr. Harry E. Bacon, Philadelphia, read a paper on "Anorectal Operative Procedures with Special Reference to the Avoidance of Pain, Based on a Series of 1,000 Cases." Discussed by Drs. Emil Granet, New York; Henry Raile, Salt Lake City; Malcolm R. Hill, Los Angeles; Louis J. Hirschman, Detroit; Arthur S. Calman, New York, and Harry E. Bacon, Philadelphia.

Dr. Horace W. Soper, St. Louis, read a paper on "Megacolon." Discussed by Drs. Sara M. Jordan, Boston; J. Arnold Bargen, Rochester, Minn., and Horace W. Soper, St. Louis.

FRIDAY, JUNE 14—MORNING

The following officers were elected: chairman, Dr. Frank C. Yeomans, New York; vice chairman, Dr. Walter L. Palmer, Chicago; secretary, Dr. J. Arnold Bargen, Rochester, Minn.; executive committee, Dr. Descum C. McKenney, Buffalo; Dr. A. H. Aaron, Buffalo, and Dr. Frank C. Yeomans, New York; delegate, Dr. Louis A. Buie, Rochester, Minn.; alternate, Dr. Emmett H. Terrell, Richmond, Va.; chairman of Committee on Section Exhibit, Dr. Sara M. Jordan, Boston.

Drs. William Bennett Bean and Tom Douglas Spies, Cincinnati, presented a paper on "Vitamin Deficiencies in Diarrheal States."

Dr. Garnett Cheney, San Francisco, read a paper on "The Clinical Value of Vitamin K."

These two papers were discussed by Drs. Thomas T. Mackie, New York; Donald T. Chamberlin, Boston; Mandred W. Comfort, Rochester, Minn.; John L. Kantor, New York; William Bennett Bean, Cincinnati, and Garnett Cheney, San Francisco.

Dr. Mandred W. Comfort, Rochester, Minn., read a paper on "The Use and Significance of Tests of Pancreatic Function."

Dr. Jacob Meyer, Chicago, read a paper on "The Clinical Significance of Salivary, Gastric and Pancreatic Secretion in Old Age."

These two papers were discussed by Drs. Joseph S. Diamond, New York; A. C. Ivy, Chicago; Edward S. Emery Jr., Boston; John L. Kantor, New York; Heinrich Necheles, Chicago; A. H. Aaron, Buffalo; Mandred W. Comfort, Rochester, Minn., and Jacob Meyer, Chicago.

Drs. Maurice Feldman and Samuel Morrison, Baltimore, presented a paper on "The Management of Gallbladder Based on a Cholecystographic Classification."

Dr. Moses Behrend, Philadelphia, read a paper on "Diseases of the Common Bile Duct and Its Relation to the Gastrointestinal Tract."

Dr. Emmanuel Deutsch, Boston, read a paper on "A Fractional Bromsulphalein Test Compared to Other Liver Function Tests for Residual Liver Damage."

These three papers were discussed by Drs. Max Thorek, Chicago; Moses Paulson, Baltimore; J. Russell Twiss, New York; Julius Friedenwald, Baltimore; S. Allen Wilkinson Jr., Boston; Mandred W. Comfort, Rochester, Minn.; A. J. Atkinson, Chicago; Henry A. Rafsky, New York; A. F. R. Andresen, Brooklyn; Maurice Feldman, Baltimore; Moses Behrend, Philadelphia, and Emmanuel Deutsch, Boston.

SECTION ON RADIOLOGY

WEDNESDAY, JUNE 12—MORNING

The meeting was called to order at 9 o'clock by the chairman, Dr. Merrill C. Sosman, Boston.

Dr. Lyndon E. Lee Jr., Wrentham, Mass., read a paper on "Medication in the Control of Pain in Terminal Cancer with Reference to the Study of Newer Synthetic Analgesics." Discussed by Drs. David I. Macht, Baltimore, and Lyndon E. Lee Jr., Wrentham, Mass.

Dr. Francis C. Grant, Philadelphia, read a paper on "Surgical Methods for the Relief of Pain." Discussed by Drs. Byron Stookey, New York, and Francis C. Grant, Philadelphia.

Drs. Eugene T. Leddy and Herman J. Moersch, Rochester, Minn., presented a paper on "Roentgen Therapy for Bronchiogenic Carcinoma." Discussed by Dr. Maurice Lenz, New York.

Dr. William Stuart Wallace, Durham, N. C., read a paper on "Studies in Radiation Sickness: Variations in the Intestinal Pattern in Sickness Accompanying Protracted Irradiation of Deep-Seated Tumors." Discussed by Drs. Ross Golden, New York; Virgil H. Moon, Philadelphia; Morton L. Levin, Albany, N. Y., and William Stuart Wallace, Durham, N. C.

Drs. Virgil H. Moon, Karl Kornblum and David R. Morgan, Philadelphia, presented a paper on "The Nature and Pathology of Radiation Sickness." Discussed by Drs. Charles L. Martin, Dallas, Texas; David I. Macht, Baltimore; Ross Golden, New York; Moses F. Lubell, Waterville, Maine; Robert P. Noble, Raleigh, N. C., and Virgil H. Moon, Philadelphia.

Dr. William E. Costolow, Los Angeles, read a paper on "Treatment of Uterine Fibromyomas." Discussed by Drs. William P. Healey, New York; Channing W. Barrett, Chicago; Arthur H. Curtis, Chicago, and William E. Costolow, Los Angeles.

THURSDAY, JUNE 13—MORNING

The following officers were elected: chairman, Dr. Raymond C. Beeler, Indianapolis; vice chairman, Dr. Ralph S. Bromer, Bryn Mawr, Pa.; secretary, Dr. John T. Murphy, Toledo, Ohio; delegate, Dr. Edward H. Skinner, Kansas City, Mo.; alternate, Dr. Eugene P. Pendergrass, Philadelphia; representative to the Board of Radiology, Dr. George W. Holmes, Boston.

Dr. Merrill C. Sosman, Boston, read the chairman's address, entitled "Subclinical Mitral Disease."

Dr. Robert E. Gross, Boston, read a paper on "Experiences with Surgical Treatment of the Patent Ductus Arteriosus: A Summary of Nine Cases." Discussed by Dr. Claude S. Beck, Cleveland.

Drs. Eugene C. Eppinger and C. Sidney Burwell, Boston, presented a paper on "The Mechanical Effects of Patent Ductus Arteriosus on the Heart and Their Relation to X-Ray Signs." Discussed by Drs. William D. Stroud, Philadelphia; Harry Vesell, New York; Maude E. S. Abbott, Montreal; M. J. Shapiro, Minneapolis; Harold E. B. Pardee, New York; William J. Kerr, San Francisco; Arthur E. Strauss, St. Louis; Robert E. Gross, Boston, and C. Sidney Burwell, Boston.

Dr. Marshall N. Fulton, Boston, read a paper on "Aneurysm of the Ventricle of the Heart." Discussed by Drs. William J. Kerr, San Francisco; Emanuel Libman, New York; Simon Dack, New York, and Marshall N. Fulton, Boston.

Dr. Soma Weiss, Boston, read a paper on "The Heart in Nutritional Deficiencies." Discussed by Drs. Tom Douglas Spies, Cincinnati, and Norman H. Jolliffe, New York.

FRIDAY, JUNE 14—MORNING

A joint meeting was held with the Section on Laryngology, Otology and Rhinology.

Dr. Harris P. Mosher, Boston, read a paper on "Fulminating Osteomyelitis of the Frontal Bone as a Complication of Infection of the Frontal Sinus."

Dr. A. S. MacMillan, Boston, read a paper on "Radiologic Aspects of Osteomyelitis of the Frontal Bone."

These two papers were discussed by Drs. Arthur C. Jones, Boise, Idaho; Joseph E. J. King, New York; Samuel R. Skillern Jr., Philadelphia; Cornelius G. Dyke, New York; Harris P. Mosher, Boston, and A. S. MacMillan, Boston.

Dr. Gordon F. Harkness, Davenport, Iowa, read a paper on "The Complications of Acute Mastoid Surgery."

Dr. Vincent C. Johnson, Ann Arbor, Mich., read a paper on "Roentgen Signs of Mastoiditis and Its Complications."

These two papers were discussed by Drs. Isidore Friesner, New York; Frederick M. Law, New York; Gordon F. Harkness, Davenport, Iowa, and Vincent C. Johnson, Ann Arbor, Mich.

Dr. Charles L. Martin, Dallas, Texas, read a paper on "Radiologic Treatment of Metastatic Cervical Lymph Nodes." Discussed by Drs. James J. Duffy, New York; Douglas Quick, New York; C. A. Whitcomb, Philadelphia, and Charles L. Martin, Dallas, Texas.

SECTION ON MISCELLANEOUS TOPICS

Session on Anesthesia

THURSDAY, JUNE 13—AFTERNOON

The meeting was called to order at 2 o'clock by the chairman, Dr. Paul M. Wood, New York.

Dr. Paul M. Wood, New York, read the chairman's address.

Drs. Stuart C. Cullen, S. E. Ziffren, R. B. Gibson and H. P. Smith, Iowa City, presented a paper on "Anesthesia and Liver Injury with Special Reference to Plasma Prothrombin Levels." Discussed by Drs. Huberta M. Livingstone, Chicago; Milton C. Peterson, New York; Max H. Weinberg, Pittsburgh, and Stuart C. Cullen, Iowa City.

Drs. E. A. Rovenstine and John Adriani, New York, presented a paper on "Studies on the Absorption of Carbon Dioxide from Anesthetic Mixtures." Discussed by Drs. Ralph M. Waters, Madison, Wis., and John Adriani, New York.

Drs. Ralph M. Tovell and Charles B. Hinds Jr., Hartford, Conn., presented a paper on "Abdominal Blocks in Conjunction with General Anesthesia for Upper Abdominal Surgery." Discussed by Drs. John S. Lundy, Rochester, Minn.; Robert L. Patterson, Pittsburgh, and Ralph M. Tovell, Hartford, Conn.

Dr. Lloyd H. Mousel, Rochester, Minn., read a paper on "The Anesthetist's Part and Opportunity in the Diagnosis and Treatment of Postoperative Atelectasis." Discussed by Drs. U. H. Eversole, Boston; Herman J. Moersch, Rochester, Minn.; F. Elmore Hubbard, Montclair, N. J., and Lloyd H. Mousel, Rochester, Minn.

Dr. Meyer Saklad, Providence, R. I., read a paper on "Criteria in the Choice of Anesthesia." Discussed by Drs. A. H. Miller, Providence, R. I.; Charles F. McCuskey, Glendale, Calif., and Meyer Saklad, Providence, R. I.

WOMAN'S AUXILIARY

Louisiana

The auxiliary to the Orleans Parish Medical Society elected Mrs. A. F. Herbert president for 1940. During the past year the auxiliary was hostess to the doctors' wives who attended the meeting of the American College of Physicians and the meeting of the New Orleans Graduate Assembly. The auxiliary also assisted in entertaining visitors to the Southern Sectional Meeting of the American College of Surgeons in New Orleans January 17-19. The auxiliary has collected funds to help a physician's widow who was in need.

New Hampshire

The woman's auxiliary to the New Hampshire Medical Society held its fifteenth annual meeting in Manchester, May 14-15; among the speakers were Dr. Nathan B. Van Etten, President-Elect of the American Medical Association; Dr. George C. Wilkins, president, New Hampshire State Board of Health, Manchester, who discussed the "Benevolence Fund of the New Hampshire Medical Society," and Kenneth N. Atkins, M.A., professor of bacteriology at Darmouth Medical School, Hanover, N. H.

Ohio

An auxiliary to the Ohio State Medical Association was organized in Cincinnati, May 15. Mrs. David W. Thomas, Lock Haven, Pa., first vice president and chairman, organization committee, Woman's Auxiliary to the American Medical Association, addressed more than 100 women at the organization meeting. The officers elected for the new organization were: Mrs. J. E. Purdy, Canton, president; Mrs. Horace Tangeman, Cincinnati, first vice president; Mrs. J. L. Stevens, Mansfield, secretary-treasurer.

Pennsylvania

At a meeting of the auxiliary to the Chester County Medical Society in West Chester, January 16, Mrs. Joseph Scattergood Sr. reviewed "The Tree of Life," by Elizabeth Page.

Major Edward A. Davies, 315th Infantry Reserve, gave an address on "The European Kaleidoscope" before a joint meeting of the Delaware County Medical Society and its auxiliary in Chester recently. The auxiliary has donated subscriptions to *Hygeia* to public reading centers in Delaware County.

At a recent meeting of the auxiliary to the Lycoming County Medical Society in Williamsport, Mr. Joseph Schmucker and Mr. Theodore Walters of the Williamsport Police Department spoke on fingerprinting, giving illustrations by means of slides and photographs.

At a recent meeting of the auxiliary to the Philadelphia County Medical Society, Dr. Myer Solis-Cohen spoke on medical benevolence; other recent guest speakers have been Mrs. John H. Doane, president of the auxiliary to the Medical Society of the State of Pennsylvania; Dr. Francis F. Borzell, president-elect of the Medical Society of the State of Pennsylvania, and Miss Besse Howard, director of the Pennsylvania Branch of the League of Nations Association.

The auxiliary to the Dauphin County Medical Society met in Harrisburg February 27. Dr. Eleanor R. Stein discussed the value of regular physical examinations on school children.

Mrs. John H. Doane, president of the auxiliary to the Medical Society of the State of Pennsylvania, spoke on the work of the auxiliary at a joint meeting of the auxiliaries to the Tioga and Bradford County medical societies in Troy.

The woman's auxiliary to the Lehigh County Medical Society recently donated $100 to the Allentown Community Chest, $25 to Girl's Haven, a recreational center for underprivileged girls, and $10 to the Red Cross Relief Fund; the auxiliary also secured 312 subscriptions to *Hygeia* during the recent Hygeia campaign; at a past president's party in April, twenty-one past presidents of the auxiliary were present.

Dr. and Mrs. Augustus S. Kech, Altoona, entertained the Blair County Medical Society and its auxiliary in honor of Mrs. Rollo K. Packard, president of the auxiliary to the American Medical Association, January 17.

West Virginia

Miss Dorothea Campbell, of the West Virginia State Health Department, spoke on state health laws at the January meeting of the auxiliary to the Kanawha County Medical Society in Charleston; thirty-five members attended.

Mrs. Harold H. Golz spoke on the prevalence, symptoms and diagnosis of cancer at a meeting of the auxiliary to the Harrison County Medical Society, Clarksburg, January 4.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Society News.—The Craighead-Poinsett County Medical Society was addressed recently by Drs. Duane M. Carr and Conley H. Sanford, both of Memphis, Tenn., on "Role of Amebiasis in Chronic Digestive Disturbances" and "Injuries to the Chest" respectively.——Dr. Richard E. Ching, Memphis, discussed "Blood Pressure" before the Mississippi County Medical Society, May 7, and Dr. Gilbert J. Levy, Memphis, "Certain Drugs in the Treatment of Meningitis."—— The speakers before the Benton County Medical Society in Gentry, May 9, were Drs. Roy E. Myers and A. M. Gregg, both of Joplin, Mo., on hyperinsulinism and hyperthyroidism, respectively.

CALIFORNIA

Sale of Sobisminol Restricted.—Because of the dangers involved in self administration of sobisminol, the California State Board of Health has adopted regulations that prohibit the sale of the drug except on written prescription of a duly licensed physician. Manufacturers of the product are also required to provide full information relative to the use of the drug in their products.

Another Symphony Orchestra.—The *Bulletin* of the San Francisco County Medical Society announces the recent formation of a "Doctors' Symphony Orchestra." Officers are Drs. Joseph L. McCool, president; Leo Eloesser and J. F. Steffan, D.D.S., vice presidents, and Dr. Donald R. Pratt, secretary-treasurer, all of San Francisco. About thirty-five physicians and dentists attended the first rehearsal at the home of the county medical society, May 16.

New State Director of Health.—Dr. Bertram P. Brown, Los Angeles, has been appointed director of the California State Department of Public Health to succeed Dr. Walter M. Dickie, San Francisco. Dr. Brown graduated at University and Bellevue Hospital Medical College, New York, in 1914. He is 48 years of age. Dr. Dickie served as chief of the division of venereal disease control in 1919, but this activity ceased in 1920 on account of lack of funds, according to *California and Western Medicine*. In 1920 he was named secretary and executive officer of the state board of health, holding this title until 1929, when he was appointed director of public health. He held this position until 1931. In 1935 he was again named health director.

DISTRICT OF COLUMBIA

Annual Meeting of Former Interns.—The twenty-first annual session of the Association of Former Interns of Freedmen's Hospital was held at the hospital, Washington, June 4-6. The speakers included:

Dr. Harry Maceo Williams, Baltimore, The Druid Health Center.
Dr. Harry M. Robinson, Baltimore, Reactions from the Arsenicals.
Dr. Joseph E. Moore, Baltimore, Determination of Cure in Syphilis.
Dr. William Montague Cobb, Erect Posture as a Key to Human Anatomy.
Dr. Samuel L. Bullock, Cases Illustrating Pitfalls in the Diagnosis of Appendicitis.
Dr. George M. Leiby, Epidemiology of Syphilis.
Dr. Perrin H. Long, Baltimore, Clinical Evaluation of the Use of Sulfanilamide, Neoprontosil, Sulfapyridine and Sulfathiazole in the Treatment of Infections.
Dr. Richard W. TeLinde, Baltimore, Organic Causes of Uterine and Genital Bleeding.
Dr. Charles R. Drew, Controlled Fluid Therapy.
Dr. Paul F. Dickens, Diagnosis and Treatment of the Anemias.
Dr. Edward Gaylord Howell, New Brunswick, N. J., Treatment of Chronic Alcoholism.

FLORIDA

State Medical Election.—Dr. Walter C. Jones Jr., Miami, was chosen president-elect of the Florida Medical Association at its recent annual session and Dr. John S. Turberville, Century, was inducted into the presidency. Vice presidents are Drs. John R. Boling, Tampa; Ferdinand Richards, Jacksonville, and Erasmus B. Hardee, Vero Beach, and Dr. Shaler A. Richardson, Jacksonville, was reelected secretary-treasurer. The 1941 meeting will be in Jacksonville.

Drs. Arce and Campos Honored.—A fishing party and dinner was given in Venice, June 7, by Dr. Fred H. Albee in honor of Dr. José Arce, dean of the faculty of medical science and professor of the surgical clinic, University of Buenos Aires, Argentina, and Dr. Oswaldo P. Campos, orthopedic surgeon of Rio de Janeiro. Among the guests were Drs. Frank D. Dickson, Kansas City, Mo.; Oscar L. Miller, Charlotte, N. C.; Edward William Alton Ochsner, New Orleans, and Joseph F. McCarthy, New York. Dr. Arce will preside at the next congress of the Pan American Medical Association in Buenos Aires, August 1941, at which time the new medical school of the University of Buenos Aires will be opened.

GEORGIA

Fifty Years of Practice.—Dr. William R. Camp, Fairburn, celebrated his fiftieth year in the practice of medicine recently. ——Recently Dr. Robert E. Adair, Cartersville, marked his completion of fifty years in the practice of medicine.

District Meeting.—The Seventh District Medical Society was addressed in Cedartown recently, among others, by Drs. Ben H. Clifton, Atlanta, on "Management and Treatment of Lung Abscesses"; Joseph Yampolsky, Atlanta, "Present Status of Chemotherapy in Pneumococcal Infections with Special Emphasis on the Use of Sulfapyridine and Sulfathiazole," and Robert F. Norton, Rome, "Etiologic Factors of Human Sterility in the Male."

Public Health Meeting.—The Georgia Public Health Association held its annual meeting at the Ansley Hotel, Atlanta, May 23-25, under the presidency of William H. Weir, Atlanta. Among the speakers were:

John C. Dixon, Chicago, Rosenwald Fund, A Layman Looks at the Health Problems of Rural Georgia.
William W. Cort, Ph.D., Baltimore, Johns Hopkins School of Hygiene and Public Health, Newer Knowledge About Hookworms and Hookworm Disease.
Dr. Eugene L. Bishop, Chattanooga, director of health, Tennessee Valley Authority, Some Health Implications of Regional Water Control.
Dr. William W. Bauer, Chicago, American Medical Association, Healthier Health Meetings.
Dr. Joseph W. Mountin, Washington, D. C., Public Health Administration.

Dr. John R. Evans, Decatur, health commissioner of DeKalb County, was elected president of the association.

IDAHO

Postgraduate Lectures.—The state division of public health sponsored its third annual postgraduate lecture tour in April. Meetings were held at Idaho Falls, Twin Falls, Boise, Lewiston and Coeur d'Alene. The speakers were members of the faculty of the University of Oregon Medical School, Portland: Drs. Howard C. Stearns, Morris L. Bridgeman and Joyle Dahl.

ILLINOIS

Care for the Medically Indigent.—If a person becomes sick in Illinois and is unable to pay for necessary medical care, although otherwise self supporting, the county of residence may be required to compensate the attending physician for such services as have been previously authorized by the supervisor of the poor. To this effect was a recent decision of the Appellate Court of Illinois, fourth district, in the case of *Buckmaster et al.* v. *Effingham County*, 23 N. E. (2d) 747, 302 Ill. App. 353. The appellants in this case, a group of physicians, after being duly authorized, treated the minor child of a day laborer who was financially able to provide his family with all the necessities of life other than medical care. The court held that under the Illinois law the county must pay for the services rendered by these physicians.

Chicago

Personal.—Dr. Ludvig Hektoen, professor emeritus of pathology, University of Chicago School of Medicine and Rush Medical College, was awarded the honorary degree of doctor of science by the university, June 11, "in recognition of his scholarly achievements in basic science and his distinguished service to the university and to medicine as a great teacher, editor and administrator." Dr. Hektoen since 1937 has been executive director of the National Advisory Cancer Council of the U. S. Public Health Service.

Annual Prize of Chicago Surgical Society.—The second annual prize of $250 of the Chicago Surgical Society was given to Dr. Leon J. Aries for a paper entitled "Experimental Analysis of the Growth Pattern and Rates of Appositional and Longitudinal Growth in the Rat Femur" and Dr. Carl Ireneus Jr. for a paper on "Experimental Bile Pancreatitis with Special Reference to Regeneration (Recovery) and to the Toxicity of the Hemorrhagic Exudate." The papers were presented at the meeting of the society May 10. Dr. Aries graduated at the University of Illinois College of Medicine, Chicago, in 1932, and Dr. Ireneus at the University of Illinois College of Medicine in 1936.

KENTUCKY

Annual Section Meeting.—The Eye, Ear, Nose and Throat Section of the Kentucky State Medical Association, which convenes separately from the association, met in Louisville, May 10. Dr. Albert C. Furstenberg, Ann Arbor, Mich., was the guest speaker on "Ménière's Disease." Other speakers included Drs. Roy Glenwood Spurling, on glossopharyngeal neuralgia; Melvin Clinton Baker, reflex neuralgias incident to disease conditions in the head; Adolph O. Pfingst, cowpox infection of the eyes, and Joseph D. Heitger, management of nasal sinus disease. All are of Louisville.

Society News.—Lieut. Col. Edgar E. Hume, former librarian of the Army Medical Library, addressed the Innominate Society, Louisville, recently on "The Army Medical Library of Washington and Its Collection of Early Kentuckiana."——Drs. William T. McConnell and Granville S. Hanes addressed the Jefferson County Medical Society, Louisville, May 6, on "The Cervix and Its Relation to Childbirth" and "Diseases Affecting the Terminal Bowel" respectively.——Dr. Emmet F. Horine addressed the Louisville Medico-Chirurgical Society, May 24, on "Paroxysmal Tachycardia and Paroxysmal Auricular Fibrillation."

MASSACHUSETTS

Winner of Automobile at Annual Session.—Dr. William Parsons Boardman, professor of dermatology, Tufts College Medical School, Boston, was awarded a 1940 Oldsmobile four door sedan at the annual session of the American Medical Association June 10-14. Dr. Boardman held the lucky number in a drawing contest for which all Fellows registered at the convention were eligible.

MICHIGAN

Upper Peninsula Meeting.—The Upper Peninsula Medical Society will hold its annual meeting in Menominee, July 10-11. The session will open with a testimonial luncheon to officers of the state medical society with addresses by Drs. Burton R. Corbus, Grand Rapids, president, and Louis Fernald Foster, Bay City, secretary. Speakers on the scientific program will include:

Dr. Albert H. Montgomery, Chicago, Abdominal Conditions in Children.
Dr. Vincent J. O'Conor, Chicago, Recent Progress in Urology.
Dr. Rollin T. Woodyatt, Chicago, Diabetes.
Dr. Lloyd E. Hamlin, Norway, Silicosis.
Dr. William L. Sherman, Detroit, Anuria.
Dr. LeMoyne Snyder, Lansing, Medicolegal Problems.
Dr. Elmer L. Sevringhaus, Madison, Wis., Treatment of the Menopause.
Dr. Lemuel D. Smith, Milwaukee, Fractures of the Hip.

A luncheon and roundtable discussion on laboratory problems will conclude the meeting. At the annual banquet Wednesday evening, Dr. Rosco G. Leland, Chicago, will speak on "Health of the American People."

MINNESOTA

Annual Meeting of Radiologists.—Dr. Harry M. Weber, Rochester, was elected president of the Minnesota Radiological Society at its twelfth annual meeting in Rochester recently; other officers are Drs. Gustav T. Nordin, Minneapolis, vice president, and John P. Medelman, St. Paul, secretary-treasurer. The annual Carman Lecture, sponsored by the society, was presented before the Minnesota State Medical Association during its annual meeting by Dr. Bernard H. Nichols, Cleveland, on "Indications for the Use of Excretory Urography in Diagnosis." At the dinner meeting of the radiological society Dr. Nichols spoke on "The Future of Radiology."

MISSOURI

State Medical Election.—Dr. Robert B. Denny, Creve Coeur, was named president-elect of the Missouri State Medical Association at its annual meeting in Joplin, May 1, and Dr. Cyrus E. Burford, St. Louis, was installed as president. Mr. Elmer H. Bartelsmeyer, St. Louis, is the executive secretary. The next annual session will be in St. Louis.

Beaumont the Soldier.—The Lloyd R. Boutwell Post number 136, American Legion, made up of physicians and dentists, held services, May 30, at the grave of Dr. William Beaumont, St. Louis. William R. Gentry, a St. Louis attorney, gave the principal address entitled "Beaumont the Soldier." Dr. Beaumont was surgeon in the medical corps of the U. S. Army from 1812 to 1840 and a veteran of the war of 1812 and the Indian wars of 1827-1832.

Society News.—The Kansas City Society of Obstetrics and Gynecology was addressed, May 9, by Drs. Dwight T. Van Del on "Use of Testosterone Propionate in the Suppression of Lactation"; Harry B. Levey, "Delivery of a Primipara with Congenital Absence of the Rectum," and LeRoy Goodman, "Effect of Estrogenic Substances on Adenomyosis of the Uterus."——The Jackson County Medical Society was addressed, May 28, by Drs. William W. Buckingham and Victor B. Buhler, Kansas City, on "Pitfalls in the Diagnosis of Tuberculosis."——Dr. Theodore H. Saferstein discussed "Hypothyroidism" before the Buchanan County Medical Society in St. Joseph, May 8.——Dr. Robert L. Sanders, Memphis, Tenn., discussed problems of peptic ulcer before the Kansas City Surgical Society, May 23.

NEW JERSEY

State Medical Election.—Dr. Watson B. Morris, Springfield, became president of the Medical Society of New Jersey at the annual meeting in Atlantic City, June 4-6, and Dr. Thomas K. Lewis, Camden, president-elect. Dr. Elias J. Marsh, Paterson, was elected first vice president and Dr. Ralph K. Hollinshed, Westville, second vice president.

NEW YORK

Society News.—Drs. Albert Vander Veer and William A. Milner addressed the Medical Society of the County of Albany, June 19, on "Traumatic Asphyxia" and "Modern Methods of Handling Prostatic Obstruction" respectively.——Dr. Harvey B. Matthews, Brooklyn, addressed the recent quarterly meeting of the Suffolk County Medical Society in Smithtown on "Obstetric Shock."

Industrial Physicians Honor Dr. Gardner.—The American Association of Industrial Physicians and Surgeons, during its annual meeting in New York, June 6, presented the annual William S. Knudsen Award for outstanding achievement in industrial medicine to Dr. Leroy U. Gardner, director of the Saranac Laboratory for the Study of Tuberculosis, Saranac Lake, because of advances in the knowledge of silicosis resulting from research directed by him. Born in New Britain, Conn., Dr. Gardner received his medical degree at Yale University School of Medicine, New Haven, in 1914. Following a period of graduate study Dr. Gardner joined the faculty of Harvard Medical School in 1915, returning to his alma mater in 1917. He was pathologist to the Trudeau Foundation at Saranac Lake from 1918 to 1926, when he became director of the Saranac Laboratory for the Study of Tuberculosis. Since 1936 he has also been director of laboratories of the Trudeau Foundation.

New York City

Personal.—Dr. Fred H. Albee received the honorary degree of doctor of science at the annual commencement exercises of Rutgers University, New Brunswick, N. J., in recognition of his work in the fields of surgery and rehabilitation.——The alumni association of the De Lamar Institute of Public Health of Columbia University gave a dinner, May 2, in honor of Dr. Haven Emerson, whose approaching retirement as head of the institute was recently announced.——Drs. John M. Converse, New York, and Edgar A. Kahn, Ann Arbor, Mich., left during the week of June 10 for service with the American Hospital at Neuilly, near Paris.

Leslie Dana Gold Medal Awarded.—John M. Glenn, LL.D., New York, honorary vice president of the National Society for the Prevention of Blindness, was presented with the Leslie Dana Gold Medal, June 11, at the annual meeting of the Association for Research in Ophthalmology in New York. Mr. Glenn was selected by the St. Louis Society for the Blind through which the medal is offered by Mr. Leslie Dana of St. Louis. The medal is given on the recommendation of the research association for outstanding achievements in the prevention of blindness and the conservation of vision. Mr. Glenn has been identified with the organized movement for the protection of eyesight in America since its beginning in 1908. He was admitted to the bar in 1882. From 1898 to 1907 he was a member of the board of supervisors, Baltimore City Charities, serving as president from 1904 to 1907. From 1907 to 1931 he was general director of the Russell Sage Foundation.

Museum of Health Elects Officers.—Officers for the American Museum of Health, which is to be established as a permanent museum with certain exhibits now in the Medicine and Public Health Building at the World's Fair as a nucleus, were recently elected. Mr. George McAneny, chairman of the

board of the Title Guarantee and Trust Company, was made president and Mr. Frederick Osborn, a director of numerous corporations and trustee of various institutions, vice president. Louis I. Dublin, Ph.D., vice president of the Metropolitan Life Insurance Company, became chairman of the board of directors and Mr. Homer N. Calver, formerly secretary of the American Public Health Association, was elected secretary. Dr. Victor G. Heiser was elected to the board of directors. The museum of health sponsored a number of exhibits in the medical building at the fair in 1939 and again this year. According to the announcement, Mayor La Guardia has promised to make available a building for the permanent museum. Plans of the museum call for a broad program of health education, it was said. These include traveling exhibits to rural communities and exhibits for the use of schools, colleges, official and voluntary medical and health agencies and other organizations.

NORTH CAROLINA

State Medical Election. — Dr. Franklin Webb Griffith, Asheville, was named president-elect of the Medical Society of the State of North Carolina at its recent meeting in Pinehurst and Dr. Hubert B. Haywood, Raleigh, was installed as president. The 1940 session will again be held in Pinehurst.

Twenty-Five Years with Health Department. — Dr. George M. Cooper, assistant state health officer and director of the division of preventive medicine and health education in the state department of health, Raleigh, was given a silver inkstand as a memento by his associates, May 1, to mark his twenty-fifth anniversary with the department. Dr. Cooper began his work as director of rural sanitation, now called county health work, and later directed school health work for several years. He was made assistant state health officer in 1923. At various times he has also directed maternal and child health services and has acted as state health officer.

NORTH DAKOTA

State Medical Election. — Dr. Frederick W. Ferguson, Kulm, was chosen president of the North Dakota State Medical Association at the annual meeting in Minot, May 6, and Dr. Cyril J. Glaspel, Grafton, was installed as president. Drs. Alfred R. Sorenson, Minot, and Frank I. Darrow, Fargo, were elected vice presidents and Dr. Leonard W. Larson, Bismarck, secretary.

OREGON

Personal.—Dr. Courtney M. Smith, recently assistant health officer of Portland, has been appointed director of maternal and child health for Alaska.——Dr. Roy A. Payne, Portland, has been appointed to the state board of health to succeed Dr. Robert L. Benson, Portland.

Southern Oregon Meeting.—The annual meeting of the Southern Oregon Medical Society was held in Ashland, May 14, with the following speakers, all of Portland: Drs. Banner R. Brooke, "Examination, Diagnosis and Treatment of the Diarrheas"; Lyle B. Kingery, "Diagnostic Value of Certain Cutaneous Symptoms"; Noble Wiley Jones, "The Problem of Atherosclerosis and Atherosclerotic Heart Disease," and Eugene W. Rockey, "Biliary Tract Surgery." In addition, Dr. Charles E. Hunt, Eugene, president of the Oregon State Medical Society, addressed the meeting.

PENNSYLVANIA

Society News.—Dr. Oscar V. Batson, Philadelphia, addressed the Dauphin County Medical Society, Harrisburg, June 4, on "Speech and Hearing Defects."——Drs. George Crile Jr. and Ernest P. McCullagh, Cleveland, were guests at the annual spring clinic of the Lycoming County Medical Society, Williamsport, June 7, conducting clinics and speaking on "Diagnostic and Surgical Aspects of Jaundice" and "Clinical Values of Testicular Hormones" respectively.——At a meeting of the Westmoreland County Medical Society, New Kensington, June 18, the speakers were Drs. Robert C. Grauer, Pittsburgh, on "Mediastinal Parathyroid Adenoma with Recovery"; William T. Holland, Springdale, "Present Status in the Treatment of Pneumonia," and Charles L. Hobaugh, New Kensington, "A Case of Papillary Cyst Adenoma."

Philadelphia

Dr. Tracy Honored.—Dr. Martha Tracy, assistant director of public health of Philadelphia and retiring dean of the Woman's Medical College of Pennsylvania, was honored at a dinner recently. The speakers included Mayor Lamberton; Dr. Hubley R. Owen, director of public health; Marion Edwards Park, LL.D., president of Bryn Mawr College; Drs. William Pepper and William N. Parkinson, deans, respectively, of the medical schools of the University of Pennsylvania and Temple University. Dr. Tracy took her medical degree from the Woman's Medical College of Pennsylvania in 1904 and the degree of doctor of public hygiene from the University of Pennsylvania in 1917. She has been associated with the woman's college since 1913, as professor of physiologic chemistry, professor of hygiene, professor of preventive medicine and since 1918 dean. Early this year Dr. Tracy was appointed assistant director of public health of Philadelphia but continued her duties as dean until the end of the college year.

Society News.—At a meeting of the Obstetrical Society of Philadelphia recently the speakers were Drs. Bernard Mann, David R. Meranze and Benjamin Leff on "Ovarian Pregnancy" and Henry D. Lafferty, "Sudden Death During or Immediately Following Labor."——Speakers before the Philadelphia Laryngological Society, April 2, were Comdr. Travis S. Moring, U. S. Naval Hospital, Philadelphia, on "Treatment of Purulent Maxillary Sinusitis"; Lieut. Comdr. Clifford A. Swanson, U. S. Naval Dispensary, Washington, D. C., "Roentgen Ray Therapy of Acute Otitis and Acute Mastoiditis," and Rear Admiral Ross T. McIntire, surgeon general, U. S. Navy, "Problems that the Specialist in Otolaryngology Meets in the Navy."

Pittsburgh

Cancer Meeting for the Public.—A public meeting on cancer was arranged by the Allegheny County Medical Society, the state department of health and the Homewood-Brushton Community Council, May 28. The program of addresses was followed by a forum with questions from the audience. The speakers were:

Dr. Albert J. Bruecken, What You Should Know About Cancer.
Dr. William A. Wycoff, Cancer of the Stomach or Intestinal Tract.
Dr. Edwin P. Buchanan, Cancer of the Breast.
Dr. Lester Hollander, Cancer of the Skin and Mouth.

UTAH

Personal.—Dr. Mancel T. Mitchell, Eau Claire, Wis., has accepted a position as obstetric consultant to the division of maternal and child health in the Utah State Board of Health, Salt Lake City.

Society News.—The Carbon County Medical Society was addressed in Price, May 12, by Drs. Edward L. Van Aelstyn, Price, on streptococcic sore throat, and Dr. Frank V. Colombo, Price, "The Catabolism of Hemoglobin."——Dr. Edward C. Rosenow, Rochester, Minn., discussed "Experimental Studies on the Etiology of Influenza and Persistent Epidemic and Postoperative Hiccup" at a joint meeting of the Salt Lake, Weber and Utah county medical societies in Salt Lake City, May 3.

WISCONSIN

Personal.—Dr. Henry V. Bancroft, Blue Mounds, was honored with a scroll of appreciation by the Dane County Medical Society at a meeting in Madison, May 20. Dr. Bancroft, who is 80 years old, has been a member of the society for fifty-five years. Dr. Frank H. Lahey, Boston, was the speaker of the evening.—— Dr. Carl W. Eberbach, Milwaukee, has been appointed to the state board of health to succeed Dr. John J. Seelman, Milwaukee. His term will expire in February 1947.

Marquette Alumni Meeting.—The Marquette University School of Medicine Alumni Association presented an all-day clinic program at the school in Milwaukee, May 8. Dr. James P. Simonds, Chicago, was the speaker at a banquet in the evening on "The General Practitioner and Modern Medicine." Among the speakers on the day program were:

Dr. Armand J. Quick, Advances in Knowledge of Treatment of Hemorrhage.
Dr. Harry Beckman, Development of New Chemotherapeutic Agents.
Dr. David A. Cleveland, Surgery of the Sympathetic Nervous System.
Dr. Ronald S. Cron, Clinical Use of Female Sex Hormones.
Dr. Francis D. Murphy, Use of Sulfanilamide and Allied Compounds in Clinical Medicine.

Society News.—Dr. Alexander E. Brown, Rochester, Minn., addressed the Medical Society of Milwaukee County, Milwaukee, May 10, on "Sulfapyridine and New Compounds."—— Drs. Edward R. Krumbiegel, Milwaukee, and Edward T. Evans, Minneapolis, addressed the Chippewa County Medical Society, May 21, in Chippewa Falls on "Acute Communicable Diseases —Their Diagnosis and Management" and "Common Sense in the Treatment of Fractures" respectively.——Drs. Robert B. Malcolm, Chicago, and Millard Tufts, Milwaukee, addressed a joint meeting of the Racine, Walworth and Kenosha county medical societies in Racine, May 16, on "Tumors of the Neck" and "Clinical Aspects of Electrocardiography" respectively.——

Dr. Frederick W. Madison, Milwaukee, discussed arthritis at a meeting of the Fond du Lac County Medical Society, Fond du Lac, May 28.——Dr. Paul C. Bucy, Chicago, addressed the La Crosse County Medical Society, La Crosse, May 7, on "Early Signs and Symptoms of Brain Tumor" and "Infectious Complications Following Swimming" respectively.——Dr. Theodore L. Squier, Milwaukee, discussed allergy at a meeting of the Eau Claire-Dunn-Pepin Counties Medical Society, Eau Claire, May 27.

GENERAL

Examination in Neurologic Surgery. — The American Board of Neurological Surgery will hold its first examination to certify candidates at the University of Illinois, 804 South Wood Street, Chicago, October 18-19. Application forms and copies of the charter and by-laws may be obtained from the secretary, Dr. Roy Glenwood Spurling, 404 Brown Building, Louisville, Ky.

P. P. Jacobs Dies.—Philip P. Jacobs, Ph.D., Morristown, N. J., for many years associated with the National Tuberculosis Association, died at his home June 12 after an illness of three months, aged 61. Dr. Jacobs became assistant secretary of the tuberculosis association in 1908 and for many years had been director of personnel training and publications. He had conducted institutes for the training of tuberculosis and health workers throughout the United States since 1917. He was the author of "The Campaign Against Tuberculosis in the United States" and "The Control of Tuberculosis in the United States." In 1924 he was decorated by the Danish government in recognition of his work.

Dr. Swain Awarded Remington Medal. — Robert L. Swain, Pharm.D., New York, who recently concluded twenty years as secretary-treasurer of the Maryland Board of Pharmacy, has been awarded the Remington Medal by the New York branch of the American Pharmaceutical Association. Dr. Swain has served as chairman of the Conference of Law Enforcement Officials; president of the American Pharmaceutical Association and the National Association of Boards of Pharmacy; editor of *Drug Topics,* and deputy commissioner of food and drugs for Maryland. The medal was awarded for Dr. Swain's contributions toward uniformity and modernization of legislation governing the practice of pharmacy. It will be presented at a dinner, the date of which has not yet been announced.

Fellowships in Child Psychiatry Available. — The National Committee for Mental Hygiene announces that a limited number of fellowships have been provided by the Commonwealth Fund and other sources for training in extramural psychiatry, especially child psychiatry. The committee is to assign fellows for one or two years at a selected child guidance clinic, the term and plan of the fellowship to be determined by the needs of each fellow. Candidates for these awards should have had at least two years of psychiatry in an approved mental hospital in addition to other qualities fitting them for extramural service. These fellowships come in response to a definite paucity of personnel in this field, it was said. Accordingly, other conditions as to age, sex and marital status must be governed by individual cases and by current demand, according to the announcement. Requests for further information should be addressed to Dr. Milton E. Kirkpatrick, National Committee for Mental Hygiene, Room 822, 50 West Fiftieth Street, New York.

Special Society Elections.—Dr. Esmond R. Long, Philadelphia, was chosen president of the American Association of the History of Medicine at its annual meeting, May 1, and Dr. Henry E. Sigerist, Baltimore, was reelected secretary. The next annual session will be held at Atlantic City, N. J., May 4-6, 1941. The association also plans to hold a fall meeting in Cleveland October 7 this year under the auspices of the Ohio Committee for Medical History and Archives, with Dr. Howard Dittrick, Cleveland, as chairman. —— The new officers of the American Neurological Association include Drs. Harold Douglas Singer, Chicago, president; Harry C. Solomon and Gilbert Horrax, Boston, vice presidents. Dr. Henry A. Riley, New York, was reelected secretary.——Dr. Theodore Lyle Hazlett, Pittsburgh, was chosen president-elect of the American Association of Industrial Physicians and Surgeons at its annual session in New York, June 7, and Dr. Daniel L. Lynch, Boston, was installed as president. Drs. John J. Wittmer, New York, and John J. Prendergast Jr., Detroit, were made vice presidents.—Dr. William B. Castle, Boston, was elected president of the American Society for Clinical Investigation at its recent annual session. Dr. Eugene M. Landis, Charlottesville, Va., is secretary. The next annual session will be held in Atlantic City, N. J., May 5, 1941.——Dr. Thomas B. Cooley, Detroit, was named president of the American Pediatric Society at its annual session in May. Dr. Hugh McCulloch, St. Louis, is secretary.

Pacific Northwest Medical Association. — The annual meeting of the Pacific Northwest Medical Association will be held at the Davenport Hotel, Spokane, July 10-13, under the presidency of Dr. Charles E. Sears, Portland, Ore. Guest speakers will include:

Dr. Wilder G. Penfield, professor of neurology and neurosurgery, McGill University Faculty of Medicine, Montreal.

Dr. Frederick A. Coller, professor of surgery, University of Michigan Medical School, Ann Arbor.

Dr. Henry G. Poncher, associate professor of pediatrics, University of Illinois College of Medicine, Chicago.

Dr. Andrew B. Stockton, assistant clinical professor of medicine, Stanford University School of Medicine, San Francisco.

Dr. John S. Lundy, department of anesthesia, Mayo Clinic, Rochester, Minn.

Dr. Anton J. Carlson, Frank P. Hixon distinguished service professor of physiology, Division of Biological Sciences, University of Chicago.

Dr. Richard W. TeLinde, professor of gynecology, Johns Hopkins University School of Medicine, Baltimore.

Dr. Fred H. Kruse, clinical professor of medicine, University of California Medical School, San Francisco.

Dr. William Edward Chamberlain, professor of radiology and roentgenology, Temple University School of Medicine, Philadelphia.

Dr. Harold E. Robertson, pathologist at the Mayo Clinic, Rochester, Minn.

CORRECTION

First State Owned Cancer Hospital.—In a news item in THE JOURNAL, June 15, page 2393, appears the statement that the state cancer hospital of Columbia, Mo., opened April 26, "is said to be the 'first hospital ever established by a state for the exclusive care of cancer sufferers.'" The commissioner of public health of Massachusetts writes that a state cancer hospital, the Pondville Hospital, authorized by the Massachusetts legislature, was opened June 23, 1927. It has been operated continuously since that time by the Massachusetts Department of Public Health and has always been restricted exclusively to cancer patients. The present capacity of the hospital is 145 beds.

Government Services

Nurses Wanted in Panama Canal Service

The U. S. Civil Service Commission announces an open competitive examination to fill graduate nurse positions in the Panama Canal Service for general staff duty and psychiatric duty. The entrance salary is $168.75 a month, subject to a retirement deduction of 5 per cent and a deduction of $40 a month for subsistence and quarters. Applications must be filed with the commission's Washington office not later than July 22 if received from states east of Colorado; not later than July 25, if received from Colorado and states westward, and not later than August 26 if received from the Panama Canal Zone. Full information and the necessary application forms may be obtained from the secretary of the Board of U. S. Civil Service Examiners at any first or second class postoffice or from the U. S. Civil Service Commission, Washington, D. C.

Collection on Gastronomy Given to Library of Congress

A collection of books on gastronomy has been given to the Library of Congress, Washington, D. C., by Dr. Arvill W. Bitting, food technologist of San Francisco, in memory of his wife, Katherine Golden Bitting, who died in 1937. The collection was assembled during their lifelong investigations into the chemistry, bacteriology and history of foods. The Library of Congress has agreed, as an exception to its usual procedure, to establish the Katherine Golden Bitting Collection on Gastronomy as a separate unit among its collections, where it may be readily available, in conjunction with her bibliography, to present and future students in the field to which she so fruitfully dedicated her life, according to an announcement. Mrs. Bitting graduated at Purdue University, remaining there as an instructor and assistant professor in botany and biology; in 1904 she married Dr. Bitting, her lifelong collaborator in her work on foodstuffs, also at that time a member of the Purdue faculty. In 1907 both joined the staff of the bureau of chemistry of the U. S. Department of Agriculture.

Foreign Letters

LONDON

(From Our Regular Correspondent)

May 25, 1940.

Reduction of Sugar and Butter Rations

A partial failure of the sugar crop in the British West Indies and the necessity for conserving current resources have rendered necessary a reduction in the weekly sugar ration from 12 to 8 ounces. Glucose also will be rationed. The loss of Denmark and Holland as sources of butter has rendered necessary a reduction of the weekly butter ration from 8 to 4 ounces. It is also expected that the bacon ration, now 8 ounces, will soon have to be cut.

Mobile X-Ray Unit for the Army

Miss Iris Michaelis, daughter of the South African philanthropist, has presented to the British army in memory of her father a mobile x-ray unit for service at the front. It is mounted on a standard lorry chassis and electric current is obtained from a gasoline driven generator packed underneath the unit when not in use. Thus it can operate in places where there is no electrical supply. The unit also carries its own water supply in a tank underneath the vehicle, and a jack is provided to maintain absolute steadiness when at work. The interior is air conditioned and shock proof throughout. It is divided into two compartments, the larger being fitted as an x-ray operating room with a full size table, novable x-ray tube and screening stand. The other compartment can be quickly converted into a dark room. The unit was designed by Lieut.-Col. D. B. McGrigor, assisted by the manufacturers, Watson and Sons.

The Prevention and Treatment of Tetanus in the War

For the prevention and treatment of tetanus in the British army, both passive and active immunization are in use for every man. Passive immunization is produced by injecting a prophylactic dose of antitoxin as soon as possible after the man has been wounded, active immunization by two injections of formol toxoid sometime before going on active service. The value of passive immunization was shown in the last war. The few who developed the disease after a prophylactic injection usually had a long incubation period and slow onset and recovered. The disadvantages of this treatment are that the injection has to be given soon after the wound is received; in some cases it has to be repeated and serum reactions are liable to occur. Active immunization has the advantages that it can be produced before the soldier goes on active service and that the immunization probably lasts many years. But it has not yet been tested on a large scale in war. The only disadvantage is slight allergic reactions, which are attributed to a small amount of peptone present.

In an address to a medical society of the British Expeditionary Force Lieut.-Col. L. B. Cole, an authority on tetanus, recommended that antitoxin be injected intravenously as soon as possible after the man is wounded. He recommended 200,000 units as large enough to neutralize all unfixed toxin and prevent further absorption. There was no advantage in repeating the dose except in the case of severe infected wounds, when an additional 50,000 units might be given intramuscularly once a week. For control of the spasms he recommended avertin with amylene hydrate by rectum as for basal anesthesia. In severe cases this would stop the convulsion in from four to six hours, when it had to be repeated. In some cases two or three such doses daily for eight or more days might be necessary. An alternative to avertin with amylene hydrate was rectal paraldehyde in basal anesthetic doses.

Foreign Synthetic Drugs

In peace times we imported from Germany the majority of synthetic drugs. On the outbreak of war the Medical Research Council took steps, in conjunction with governmental departments and the Association of British Chemical Manufacturers, to secure that we shall not be without the important synthetic drugs hitherto obtained from abroad. Some of the British substitutes can have their identity proved by chemical means, but for others the council has thought clinical trials necessary to insure that they are equivalent in all respects to proprietary products hitherto imported under trade names. The result is that chemical names now take the place of trade names. Thus avertin has become bromethol; evipan sodium, soluble hexobarbitone. The General Medical Council will publish as an addendum to the last edition of the British Pharmacopeia, which was published in 1932, articles dealing with other foreign drugs which are now being produced or are likely soon to be produced by British manufacturers. Hitherto these have been known under registered trade names, but they will now be given official pharmacopeial names.

STOCKHOLM

(From a Special Correspondent)

April 9, 1940.

(This letter, mailed April 9 from Bergen, Norway, arrived on June 24 after passing through the German censorship, apparently by way of Salonika, Greece.)

The Fitness of Swedish Doctors for Army Service

Recent events have stressed the need for a fully documented card index of the doctors and medical students with reference to their fitness for army medical service in case of war. In October 1939 the medical societies throughout Sweden agreed to the compiling of such a card index to cover the Universities of Stockholm, Uppsala and Lund. The information collected in this index concerned, among other things, a summary of the physical condition of each doctor and medical student and the opinions of the doctors themselves as to their ability to serve in the field or undertake exacting duties in the hospital. This index sheds a most disquieting light on the high frequency of tuberculosis in the medical profession; it was far and away the most important cause of faulty health disqualifying for military service. Indeed, between 43 and 44 per cent of all the exemptions from military service were based on tuberculosis. Some form or other of heart disease came next in the list of disqualifications, but these cases were only half as numerous as those of tuberculosis. Altogether only 71 per cent of all the doctors could be considered as fit for military service. In other words, in the event of war 11 per cent of the doctors could not be called up for army service because they were women and 18 per cent because they were not fit enough. The tuberculosis rate was somewhat lower among the medical students than among the doctors, presumably because exposure to infection had not been so long on the average for the students and because there has been a marked decline in the incidence of tuberculosis in the past generation.

The Evolution of Hospital Treatment for Children

At the last annual meeting of the Swedish Association of Pediatricians Prof. Curt Gyllenswärd of Stockholm delivered a statistically inspired lecture on the evolution of children's hospitals and the social work now being done in them. It is curious how rapid and fundamental has been the revolution in Swedish hospitals for children. A generation or two ago these hospitals catered mainly to severe cases of well defined disease, whereas they are now made use of more and more for acute cases which formerly would have been treated at home unless some operation had to be performed. It might well have been thought that with birth control and the dwindling numbers of children (there are now some 2,000 fewer children in Stock-

holm than there were only ten years ago) the claims on the beds in hospitals for children would have diminished. So far from this being the case, the claims on such beds have increased by 50 per cent in the last decade.

The Passing of the Maiden Aunt

Why is the sick child, formerly nursed at home, now bundled off to a hospital at short notice and kept there till all is well again? Professor Gyllenswärd finds the answer to this question in the modern home which the mother leaves to follow some employment elsewhere and which is now bereft of the unattached maiden aunt, not to mention the grandmother, who in former days used to be considered a superfluous nuisance but who in reality often proved the mainstay of the family. Acid and angular the maiden aunt may have been, but she was more than worth her salt in the countless emergencies of a large family. Another inducement for parents to send their sick children to hospitals in Stockholm is the modesty of the charges made for their accommodation—only 2.50 kronor (60 cents) a day. Thus for a fortnight's treatment the parents have to pay only 35 kronor ($8.35) and, as a matter of fact, only 46 per cent of the children are paid for at this rate, some reduction or complete exemption being obtained for the remainder. Professor Gyllenswärd pleaded urgently for a more comprehensive and sympathetic study of the hospital child's spiritual and mental needs than has heretofore been devoted to him.

Aid for Swedish Doctors in Finland

Several members of the Swedish Medical Association have undertaken to contribute the earnings of one day a month to aid for Finland. This association has established a guaranty fund of 660,000 kronor ($157,608) for the support of the dependents of those doctors who have gone to Finland, in the event of their being killed or wounded.

BUENOS AIRES

(From Our Regular Correspondent)

May 24, 1940.

Cancerigenic Factors

Prof. Angel H. Roffo of Buenos Aires recently demonstrated that cholesterol contained in the body and in foods such as meat, fats and eggs, when activated by the ultraviolet rays of the sun, produces fluorescent and radioactive hydrocarbons of a cancerigenic character. He further called attention to his belief that the increase in the large cities of carcinoma of the respiratory organs was due to exhaust gas of motor vehicles. He was able to extract from the air of one of the busiest streets of Buenos Aires relatively large quantities of a mineral oil the absorption lines of which were contained within the same angstrom units and showed the same qualities of fluorescence as the oil which was obtainable from cotton filters placed in the pipes by which carburetors are fed. Certain quantities of mineral oil containing polycyclic hydrogens are found in the air, derived, no doubt, from the incomplete combustion not only of motors that use benzene but of Diesel motors as well. Roffo has also shown in rat experimentation that carcinoma of the lungs develops if rats are compelled to live for several months in an atmosphere contaminated by Diesel oil combustion products.

Public Health Administration in Chile

A new division concerned with the connection between nutrition and health has been created in Chile's department of public health with authority to investigate the nutritional status of the whole country. It exercises control over milk and veterinary inspection and over foods, diets, educational campaigns and laboratories. Special legal enactments are being planned with relation to the manufacture and sale of margarine and smoked fish, milk and milk products, horse meat and vinegar. At certain times in which milk production went through a crisis this branch of the health service established centers for the rationing of milk. This kept the price of milk down. At the same time an extensive campaign was conducted showing the highly nutritious value of milk. Milk served to school children will soon reach 23 per cent of such children. Breakfasts furnished to school children at present contain 271 calories.

The commission for the control of the price of drugs in general, existing since 1932, has not been able to function properly in the past. Prices and detailed specifications have now been set up for more than 2,000 medicinal products, thereby not only preventing speculation in drugs but enabling the public to obtain medicaments at a lower price than can be obtained in other countries.

A special division for the control of venereal diseases has been created in which the different health boards, the army and scientific societies are cooperating. There is no charge for treatments. These are compulsory only for the army. It is planned to place all venereal diseases under the control of the department of preventive medicine and to organize prophylactic centers in the large industries. Sex education should, it is believed, begin early, in cooperation with schools and churches. The division for venereal diseases favors the abolition of legalized prostitution.

Rabies in Argentina and Cuba

Central headquarters for rabies control in Argentina is the Instituto Antirrábico Pasteur in Buenos Aires, under the direction of Dr. Carlos Ramos Mejía. This is a municipal institute but cooperates with the National Department of Public Health, since its activities embrace the whole country. Founded in 1886, it has grown during the last two decades. In the half century intervening between 1886 and 1937 about 200,000 persons were observed, 70,000 of whom were treated. The average mortality was 3 per thousand. In 1937 more than 13,000 dogs were examined and positive infections found in about 240. By charting the possible entries by which rabid animals made their way into the city, it was found that two villages especially were responsible for rabic infection.

In Cuba, according to recent data, more than 32,000 dogs were inoculated against rabies in 1936-1937. Positive reactions were obtained in only seven of ninety-seven suspected dogs. In Cuba dead vaccines were used, which excludes the possibility of creating carriers through vaccination. Inoculation of dogs at the expense of the owner is now being required in Cuba.

Marriages

EUGENE S. HOPPENSTEIN, San Francisco, to Miss Isabel M. Armstrong of Lewiston, Idaho, in Seattle, April 3.

PHILLIP H. HALPERIN, Madison, Wis., to Miss Dorothy Milgram of Kansas City, Mo., April 9.

AUGUSTINE NOVELLO, Ashtabula, Ohio, to Miss Eleanor Eileen Finnerty of Cleveland in April.

CLAUDE C. NUCKOLS JR. to Miss Margaret Weatherwax, both of Albany, N. Y., April 20.

CHARLES J. AUCREMAN, Montpelier, Ind., to Miss Marcella Gillum of Winchester, June 6.

J. ZEB MCDANIEL to Miss Opal Lois Dowden, both of Augusta, Ga., April 13.

WILIAM J. MAUERMANN, Beloit, Wis., to Miss Lois Alton of Madison, April 2.

EUGENE B. LEY to Miss Marie Barbara Cabar, both of Detroit, June 17.

EUGENE C. SMITH to Miss Helene Sullivan, both of Flint, Mich., May 7.

VIOLET H. KIDD, Souderton, Pa., to Rev. Paul M. Scholl recently.

Deaths

John Taylor Fotheringham, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1891; Trinity Medical College, Toronto, 1891; emeritus professor of the history of medicine at the University of Toronto Faculty of Medicine; fellow of the American College of Surgeons and the American College of Physicians; was assistant director of medical service of the Second Canadian Division in France and director-general of medical service in Canada during the World War; consultant, Hospital for Sick Children and Toronto General Hospital; aged 79; died, May 9.

John Glover South, Louisville, Ky.; University of Louisville (Ky.) Medical Department, 1897; member and past president of the Kentucky State Medical Association; director of the bureau of registration and past president of the state board of health; member of the House of Delegates of the American Medical Association in 1920-1921; formerly United States Minister to Panama and Portugal; at one time health officer of Franklin County; aged 67; died, May 13.

John Herman Wylie, Peiping, China; Columbia University College of Physicians and Surgeons, New York, 1912; a medical missionary for the Board of Foreign Missions of the Presbyterian Church of the United States of America; on the staff of the Douw Hospital; aged 55; died, May 7, in a hospital at Cleveland following an operation for brain tumor.

Emil Alexius Edlen, Moline, Ill.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1892; member of the Illinois State Medical Society; at one time city physician; aged 80; formerly on the staffs of the Moline Public Hospital and the Lutheran Hospital, where he died, May 10, of uremia, myocarditis and arteriosclerosis.

Walter Scott Rountree, Birmingham, Ala.; Birmingham Medical College, 1900; member of the Medical Association of the State of Alabama; fellow of the American College of Surgeons; served during the World War; gynecologist to the Hillman Hospital; surgeon to the Norwood Hospital; aged 66; died, May 6, of cerebral hemorrhage.

Charles William Schmehl, Cleveland; University of Pennsylvania Department of Medicine, Philadelphia, 1893; member of the Medical Society of the State of Pennsylvania; past president and secretary of the Warren County Medical Society; at one time health officer of Warren, Pa.; aged 66; died, May 17, in a local hospital of pneumonia.

Wade MacMillan, Oxford, Ohio; Miami Medical College, Cincinnati, 1891; professor of orthopedic surgery at his alma mater from 1905 to 1907; for many years medical director of Miami University; aged 75; for many years surgeon to the Christ Hospital, Cincinnati, where he died, May 13, of cerebral arteriosclerosis and thrombosis.

Raymond Nazaire Filiatreau, Elwood, Ind.; Marion-Sims College of Medicine, St. Louis, 1899; University of Louisville (Ky.) Medical Department, 1900; member of the Indiana State Medical Association; served during the World War; aged 67; died, May 16, in the Mercy Hospital of pulmonary tuberculosis and diabetes mellitus.

Paul Emerson Gilmor ✠ Canal Fulton, Ohio; Western Reserve University School of Medicine, Cleveland, 1916; formerly a medical missionary; formerly county health officer; aged 50; on the associate staff of the Massillon City Hospital, where he died, May 16, of coronary heart disease.

John H. Oliver ✠ Kewanee, Ill.; Beaumont Hospital Medical College, St. Louis, 1896; past president of the Henry County Medical Society; on the staff of the Kewanee Public Hospital; aged 69; died, May 16, in the Evanston (Ill.) Hospital of coronary occlusion and arteriosclerosis.

John A. Devron ✠ New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1896; served during the Spanish-American and World wars; aged 66; died, May 13, at the Baptist Hospital of arteriosclerotic heart disease, diabetes mellitus and pneumonia.

Irving Wagner Metz, Springfield, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; member of the Illinois State Medical Society; aged 67; died, May 12, of cerebral hemorrhage, arteriosclerosis and hypertension.

Lyman Allen Steffen ✠ Antigo, Wis.; Rush Medical College, Chicago, 1912; past president of the Langlade County Medical Society; served during the World War; city health officer; on the staff of the Langlade County Memorial Hospital; aged 52; died, April 10.

William Joseph Linley, Columbia, S. C.; Medical College of the State of South Carolina, Charleston, 1892; formerly associated with the United States Public Health Service; aged 69; died, May 1, in the Anderson County Hospital, Anderson, of cerebral hemorrhage.

Joseph Ambrose Cox ✠ Albany, N. Y.; Albany Medical College, 1901; fellow of the American College of Surgeons; served during the World War; attending surgeon to St. Peter's and Brady Maternity hospitals, and Infant Home; aged 61; died, April 23.

Caleb A. Calvert, Scottsville, Ky.; Barnes Medical College, St. Louis, 1898; past president and secretary of the Allen County Medical Society; at one time county health officer; aged 63; died, May 26, of cerebral hemorrrhage and arteriosclerosis.

Herman Albert Hanser ✠ St. Louis; Missouri Medical College, St. Louis, 1898; fellow of the American College of Surgeons; for many years on the staff of the Lutheran Hospital; aged 62; died, May 28, in Flagstaff, Ariz., of heart disease.

John W. Craig ✠ Chicago; College of Physicians and Surgeons, Keokuk, Iowa, 1881; an Affiliate Fellow of the American Medical Association; member of the Iowa State Medical Society; aged 83; died, May 6, of chronic myocarditis.

Benjamin Thomas Atkins, Shallotte, N. C.; Medical College of the State of South Carolina, Charleston, 1901; aged 62; died, May 9, in the Rowan Memorial Hospital, Salisbury, of urinary extravasation with gangrene and urethral stricture.

Benjamin Franklin Easter, New Orleans; Meharry Medical College, Nashville, Tenn., 1903; aged 65; died, May 16, in the Flint Goodridge Hospital of bronchopneumonia, following a vertebral fracture received in a fall.

Wilkins McDade ✠ Minden, La.; Memphis (Tenn.) Hospital Medical College, 1909; past president and secretary of the Webster Parish Medical Society; aged 54; died, May 24, of injuries received in an automobile accident.

Pete Ernest Magoun, Vidalia, La.; University of Louisville (Ky.) Medical Department, 1906; member of the Louisiana State Medical Society; for many years parish coroner; aged 56; died, April 8, in a hospital at Natchez, Miss.

William Avery Gaylord, Pawtucket, R. I.; Harvard Medical School, Boston, 1899; member of the Rhode Island Medical Society; on the consulting staff of the Memorial Hospital; aged 65; died, May 22, of coronary thrombosis.

Richard Kring, St. Louis; Missouri Medical College, St. Louis, 1891; served during the World War; aged 76; died, May 16, in the Veterans Administration Facility, Danville, Ill., of chronic myocarditis and arteriosclerosis.

Charles Hamilton, Carlock, Ill.; College of Physicians and Surgeons, Chicago, 1895; on the staff of the Brokaw Hospital, Normal; aged 70; died, April 15, of bronchopneumonia, arteriosclerosis, cerebral thrombosis and uremia.

Benjamin Chase Grout, Berwyn, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; aged 69; died, May 12, of coronary occlusion and arteriosclerosis.

Preston Thompson, Lebanon, Mo.; Washington University School of Medicine, St. Louis, 1913; member of the Missouri State Medical Association; served during the World War; aged 51; died, April 14.

George Henry Bowles, Toronto, Ont., Canada; M.B., University of Toronto Faculty of Medicine, 1892; M.D., Victoria University Medical Department, Coburg, 1892; aged 76; died, April 10.

William Lee Patterson, El Dorado, Ark.; Memphis (Tenn.) Hospital Medical College, 1910; member of the Arkansas Medical Society; aged 60; died, May 29, of a self-inflicted bullet wound.

Samuel Victor King, Sharon, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1901; fellow of the American College of Surgeons; served during the World War; aged 63; died, April 3.

George Frederick Sneed ✠ Kirksville, Mo.; St. Louis University School of Medicine, 1926; aged 47; died, May 10, in the Barnes Hospital, St. Louis, following an operation for brain tumor.

Foster Thomas Jones, New Orleans; Meharry Medical College, Nashville, Tenn., 1917; aged 50; on the staff of the Flint Goodridge Hospital, where he died, May 28, of cerebral hemorrhage.

Riley F. Cheatham, Diamond, Mo.; St. Louis College of Physicians and Surgeons, 1903; member of the Missouri State Medical Association; aged 70; died, April 3, of carcinoma of the prostate.

John Luther Pittman, Palmetto, La.; Memphis (Tenn.) Hospital Medical College, 1908; served during the World War; aged 72; died, April 19, in the Veterans Administration Facility, Alexandria.

James Ora Pearman, Mahomet, Ill.; Rush Medical College, Chicago, 1885; aged 80; died, May 4, in the Burnham City Hospital, Champaign, following an operation for prostatic obstruction.

Ernest Rowland ✠ Liberty Grove, Md.; Baltimore Medical College, 1895; past president of the Cecil County Medical Society; aged 65; died, April 27, of chronic myocarditis and nephritis.

Robert Yates Hayne Thomas, Jacksonville, Fla.; Medical College of the State of South Carolina, Charleston, 1904; member of the Florida Medical Association; aged 63; died, April 14.

Vasco Mortimer Beecher Jr., Atlanta, Ga.; Emory University School of Medicine, Atlanta, Ga., 1937; aged 25; died, May 21, at Marianna, Fla., of injuries received in an automobile accident.

David Thomas Muir, Alden, Kan.; University of Tennessee Medical Department, Nashville, 1901; member of the Kansas Medical Society; aged 70; died in May of carcinoma of the bladder.

Francis M. Reed, Turrell, Ark. (licensed in Arkansas in 1903); aged 69; died, May 6, in St. Joseph's Hospital, Memphis, Tenn., of leukemia, chronic nephritis and bronchopneumonia.

Arthur Eugene Knoefel Sr. ✠ Black Mountain, N. C.; University of Louisville (Ky.) Medical Department, 1893; town health officer; aged 67; died, May 20, of coronary occlusion.

Arthur Joseph Babin, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1896; aged 66; died, May 19, of chronic nephritis and cirrhosis of the liver.

John D. Ball, Lexington, Mo.; Meharry Medical College, Nashville, Tenn., 1892; aged 80; died, May 23, in St. Margaret's Hospital, Kansas City, Kan., of ascending pyelonephritis.

Louis Philippe Dorval, Montreal, Que., Canada; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1903; aged 60; died, April 24.

Arthur West Allen, Austin, Minn.; Rush Medical College, Chicago, 1885; member of the Minnesota State Medical Association; aged 77; died, May 6, of carcinoma of the sigmoid.

Charles H. Lockhart ✠ Witt, Ill.; Missouri Medical College, St. Louis, 1898; on the staff of St. Francis Hospital, Litchfield; aged 68; died, May 17, of cerebral hemorrhage.

George B. Smith, Toronto, Ont., Canada; M.B., University of Toronto Faculty of Medicine, 1880; M.D., Victoria University Medical Department, Coburg, 1880; aged 88; died, May 16.

William Robert Gilbert, Tyro, Miss.; Kentucky University Medical Department, Louisville, 1904; member of the Mississippi State Medical Association; aged 61; died, April 5.

Ney Milton Salter ✠ Williams, Calif.; Northwestern University Medical School, Chicago, 1911; county health officer; served during the World War; aged 55; died, April 13.

Frank Marvin Banker, Franklin Grove, Ill.; Rush Medical College, Chicago, 1892; for many years county coroner; aged 72; died, May 30, of myocarditis and diaphragmatic hernia.

John William Hayes, Franklin, Ky.; University of Louisville (Ky.) Medical Department, 1889; member of the Kentucky State Medical Association; aged 75; died, April 10.

William T. McDonald, Vilonia, Ark. (licensed in Arkansas in 1903); member of the Arkansas Medical Society; aged 74; died, May 26, of chronic myocarditis and nephritis.

Sydney Fredrick Tichborne, Toronto, Canada; Queen's University Faculty of Medicine, Kingston, Ont., 1918; served during the World War; aged 46; died, April 4.

Richard Allen, Winchester, Ky.; University of Louisville Medical Department, 1890; aged 81; died, May 30, in the Clark County Hospital of cerebral hemorrhage.

Joseph L. Barber, Marathon, Wis. (licensed in Wisconsin in 1925); member of the State Medical Society of Wisconsin; formerly state senator; aged 76; died, April 6.

Harold Austin Smith, New York; New York Homeopathic Medical College and Flower Hospital, New York, 1920; aged 46; died, May 13, of carcinoma of the liver.

Coral Adelbert Lilly ✠ Ann Arbor, Mich.; Rush Medical College, Chicago, 1901; aged 62; died, May 3, in the University Hospital of atherosclerosis with aneurysm.

Joseph M. Campbell, East Moline, Ill.; Missouri Medical College, St. Louis, 1880; formerly St. Clair County coroner and sheriff; aged 86; died, May 15, of uremia.

Robert Nichols, Houston, Texas; Eclectic Medical University, Kansas City, Mo., 1912; aged 59; died, May 30, in the Memorial Hospital of hyperthyroidism.

George Schmucker Frank ✠ Millheim, Pa; Jefferson Medical College of Philadelphia, 1883; bank president; at one time county coroner; aged 80; died, April 13.

Lemuel K. Chandler, Tucson, Ariz.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1935; aged 31; died, May 20, of rheumatoid arthritis.

Samuel J. Drummond ✠ Casnovia, Mich.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1897; aged 73; died, April 28, of pneumonia.

Frederick Richmond Adamson, Abilene, Texas; University of Nashville (Tenn.) Medical Department, 1900; aged 66; died, May 28, of coronary occlusion.

Charles Clifton Scott, Princeton, Ill.; Rush Medical College, Chicago, 1891; member of the Illinois State Medical Society; aged 73; died, April 3.

William Canova Peterson Jr., Wilmington, N. C.; University of Virginia Department of Medicine, Charlottesville, 1917; aged 49; died, April 10.

Pietro C. Blasi, Mount Vernon, N. Y.; Regia Università degli Studi di Roma, Facoltà di Medicina e Chirurgia, Italy, 1897; aged 66; died, April 3.

Meyer Nuta, Chicago; Universitatea din Bucuresti Facultatea de Medicina, Rumania, 1901; aged 66; died, May 20, of carcinoma of the pancreas.

Israel Fred Stowe, Basco, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1910; aged 65; died, May 5, of cerebral hemorrhage.

John H. Driver, Brownsville, Texas; Arkansas Industrial University Medical Department, Little Rock, 1884; aged 83; died, April 1.

Alonzo Bowen Hyndman, Carp, Ont., Canada; McGill University Faculty of Medicine, Montreal, Que., 1915; aged 49; died, April 9.

George Edward Chappell ✠ Sacramento, Calif.; College of Physicians and Surgeons of San Francisco, 1905; aged 62; died, April 3.

Jacob Hall, Kansas City, Mo.; Eclectic Medical University, Kansas City, 1902; aged 81; died, May 7, of cerebral hemorrhage.

Laura Ewing Reading, Tampa, Fla.; Woman's Medical College of Baltimore, 1885; aged 89; died, May 12, of chronic myocarditis.

John Fletcher Douthitt, Dover, Ohio; Starling Medical College, Columbus, 1898; aged 65; died, May 6, of coronary thrombosis.

Werner Hiltpold ✠ Easthampton, Mass.; University of Vermont College of Medicine, Burlington, 1912; aged 50; died, April 5.

Joseph Walter Rogers, Macon, Ga.; Louisville (Ky.) Medical College, 1889; aged 82; died, May 1, of chronic cystitis.

Charles Henry Moncure, Orange, Va.; Medical College of Virginia, Richmond, 1880; aged 81; died, May 11, of uremia.

Frederick George Metzger ✠ Carthage, N. Y.; University of Buffalo School of Medicine, 1907; aged 57; died in April.

Jacob Coy Bucher, Alpena, Mich.; Medical College of Ohio, Cincinnati, 1878; aged 86; died, April 23, of senility.

Albert Hathaway ✠ Edon, Ohio; Rush Medical College, Chicago, 1881; aged 90; died, May 9, of heart disease.

John McLean, Hartford, Mich.; Chicago Medical College, 1873; formerly health officer; aged 100; died, April 26.

William Turner Morris ✠ Wheeling, W. Va.; Pulte Medical College, Cincinnati, 1902; aged 60; died, April 30.

Samuel Proctor Kerns ✠ Philadelphia; Jefferson Medical College of Philadelphia, 1892; aged 77; died, April 7.

Hugh Horace Ross, Seaforth, Ont., Canada; University of Toronto Faculty of Medicine, 1896; died, April 8.

J. D. L. Ball, Milton, W. Va. (licensed in West Virginia in 1888); aged 89; died, May 2, of senility.

Correspondence

FRACTURE OF THE POSTERIOR ARCH OF THE ATLAS

To the Editor:—The authors of the clinical note "Fracture of the Posterior Arch of the Atlas" (Sinberg, S. E., and Burman, M. S.: THE JOURNAL, May 18, p. 1996) present two cases with instructive roentgenograms and follow-up histories.

They describe the mechanism of the injury as pressure of the occiput on a "rigid cervical spine with the muscles of the neck relaxed." As a rule muscular fixation seems to be essential in producing a fracture of the atlas in this squeezing action. The authors are kind enough to refer to two short articles of mine on the subject, while the more detailed paper "Fractures of the Atlas Resulting from Automobile Accidents: A Survey of the Literature and Report of Six Cases" (*Am. J. Roentgenol.* **40**:867 [Dec.] 1938) apparently has escaped their attention. Sinberg and Burman conclude that fracture of the posterior arch does not seem to be an independent fracture but is associated with fractures of the cervical spine at other points. One can agree with this statement only for the majority of atlas fractures. Table IVb of my more detailed paper lists fifty-nine cases of concurrent injuries of the remaining spine, while table IVa lists forty cases of isolated fractures of the atlas, many of them confined to the posterior arch.

H. F. PLAUT, M.D., Mansfield, Ohio.

TESTS FOR CONCENTRATION OF ALCOHOL IN BLOOD

To the Editor:—The communication to this department by Dr. Leake and his associates (THE JOURNAL, March 23, p. 1098) wherein purported evidence was given to support a claim of unreliability of the Heise method for determining the concentration of alcohol in the blood has been ably answered by Dr. Heise (April 6, p. 1391) and by Dr. Harger (April 27, p. 1687). However, owing to the damage to the validity of such tests as criteria for stages of intoxication which this communication from Dr. Leake has undoubtedly caused and at the insistence of Dr. Heise, my associates and I decided to offer the following as additional refutation of Dr. Leake's claims.

Fifty specimens of human blood were taken by us over a period of two weeks from patients sent to the laboratory for various blood tests from the eight clinics which this department conducts. These patients were composed of men, women and children. Some were patients under treatment in the venereal clinic, some were diabetic patients and some were patients with nephritis.

All specimens were obtained in a deliberately careless manner. Alcohol was used to sterilize the skin thoroughly and no attempt was made to wipe the arm dry.

All specimens were distilled at the maximum rate possible—so fast that all distillates showed some degree of yellow color due to traces of picric acid carried over by the excessive rate of distillation.

All distillates were run undiluted. There was no detectable reduction of the dichromate solution in any of the fifty specimens.

Finally, three pooled 50 cc. specimens were made up to a concentration of 0.4 per cent by volume with lactic acid (twice the highest reduction claimed by Dr. Leake) and each was distilled. No detectable reduction in the undiluted distillate was observed in any of the three prepared specimens.

I have had experience with some 300 consecutive tests for drunken driving over the past three years. This, coupled with a knowledge of the literature on the subject, made Dr. Leake's contentions too fantastic to be considered valid. However, no definite effort has ever been made, to the best of my knowledge, to support the reasoning from physiologic and chemical principles involved, which make such claims as those of Dr. Leake untenable, by positive proof in the form of any significant number of tests on normal bloods. Hence the foregoing experiments.

Such communications result in charges that there is no agreement among experts as to the specificity of chemical tests for intoxication. One such published statement from a well intentioned but misinformed source can undo the results of years of painstaking work on the part of recognized authorities in this field.

DONALD F. BAVIS, B.Sc., Lincoln, Neb.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SENSITIVITY TO RAGWEEDS AND COCKLEBUR

***To the Editor:*—A patient with hay fever was found to give a strongly positive reaction to the pollens of ragweed and cocklebur, especially the latter. Should I desensitize him against both of these pollens or do you think that desensitization with ragweed alone (giant and dwarf) will build up antibodies against the proteins of cocklebur as well, as the two belong to the same botanic group (Ambrosiaceae)?**

M.D., Connecticut.

ANSWER.—Although the pollen of cocklebur is not profuse in the air, it is present in small amounts and therefore it should be incorporated in a mixture with ragweed. Because of the overabundance of ragweed, one would suggest that the mixture contain 45 per cent giant ragweed, 45 per cent small ragweed and 10 per cent cocklebur.

INTRAVENOUS ANESTHESIA

***To the Editor:*—Please send information regarding intravenous amytal as an anesthetic, indications and contraindications, dosage, dangers contingent on its use and antidotes. If there has been any intravenous anesthesia developed since that is superior, I would appreciate information on it. Is avertin with amylene hydrate as rectal anesthesia in good repute and general usage, and are methods of administration and dosage determination about the same as described in M. D. Nosworthy's "Anesthesia" published in 1935?**

George Jennings, M.D., Buhl, Idaho.

ANSWER.—Sodium amytal for intravenous administration as a general anesthetic is seldom used in surgery. It can be used safely only by those who have had much experience and are familiar with the literature concerning such use. The Council on Pharmacy and Chemistry of the American Medical Association does not recommend the use of nonvolatile barbiturate preparations in major surgical procedures. Sodium amytal is occasionally given intravenously to control the convulsions arising in association with eclampsia and tetany, in cyanotic individuals or those moribund from trauma, to control the pain of inoperable cancer, and to facilitate cystoscopic examinations and the incision of abscesses, or as a basal anesthetic.

The dose for an adult is usually 1 grain (0.065 Gm.) given in a series of graded doses. If the needle is not removed from the vein, more may be injected intravenously as necessary. Larger doses may be needed for some patients but smaller doses may suffice for others. After the first dose has been given intravenously, succeeding doses are often given to advantage through a nasal or stomach tube, the dose usually being 1 grain (0.065 Gm.) at a time, given intermittently, according to the patient's reaction.

The commonest danger is the obstruction of the respiratory passage by the tongue falling back and covering the glottis. The patient therefore should ordinarily be turned on his side or the head lowered with the jaw supported if the air passage is not clear. Like other barbiturates, sodium amytal is a respiratory depressant and any antidotes given should be those which stimulate respiration. The fall in blood pressure must be combated with circulatory stimulants and intravenous infusion of fluids. Included in the antidotes are metrazol, picrotoxin, nikethamide, ephedrine, solution of epinephrine hydrochloride, and solution of posterior pituitary U. S. P. Metrazol and picrotoxin are agents which must be used with caution. Postopera-

tive manias or excitement may require close supervision for hours. Since there is a tendency for pulmonary edema to develop after large doses of sodium amytal, administration of oxygen and carbon dioxide may be used. The patient should be turned in bed from time to time so that pulmonary edema will not develop in the dependent portion of the lung.

One of the newer and better intravenous anesthetics is pentothal sodium. It is not recommended in major operative procedures requiring long anesthesia or for office procedures.

Avertin with amylene hydrate as a rectal anesthetic is not used as much as formerly. However, it is frequently used for a basal anesthetic, supplemented by a local or general anesthetic. The doses described in M. D. Nosworthy's "Anesthesia," published in 1935, are satisfactory.

URTICARIA AND COLITIS

To the Editor:—**In April 1931 a man then 32 years old had a septic sore throat which was treated by his physician with intravenous injections of acriflavine hydrochloride 20 cc. per session. On one of these occasions the fluid was injected paravenously, intra-arterially and into the left elbow joint, with resulting severe reactions leaving the patient finally with a paralysis of the median and ulnar nerves. As the result of a law suit he was enabled to receive the best of care available and traveled all over Europe in order to get the use of his left hand back again. During all this time he refused to be given morphine for the excruciating pain and was given a combination of codeine acetylsalicylic acid and acetophenetidin. After he had spent almost two years in different institutions abroad, his hand finally had improved so much that he is able to hold a newspaper or a comb. He still cannot bind his own ties. About 1934 he noticed the appearance of hives all over his body, with temperatures up to 104 F. and glottis edema, which at one time almost necessitated a tracheotomy. Scratch and intradermal tests, however, never gave positive reactions to anything except peptones and polypeptides. After proteins had been eliminated from his diet, the hives and itching disappeared for about two weeks and returned. He has since been treated with dry peptone prepared from fibrin, histaminase, calcium gluconate (which aggravated his condition considerably while he took it), pancreas therapy, and finally old tuberculin, starting with 0.1 cc. of a 1:100,000 solution and increasing to 0.98 cc. of a 1:100 solution. While these daily injections were being given the urticaria became less and less frequent, until after eighty injections he was able to eat everything, including meats, milk and eggs, without getting a reaction. This lasted for about six months after the last injection of old tuberculin. Then he suddenly had colitis, bloody slimy diarrhea and return of his urticaria. Old tuberculin was resumed but with less success, for he had changed his town and the doctor was afraid to go ahead with a daily dose. So it was given with a four day interval for about three months. All this time the patient was watching his diet and carefully avoided milk, eggs and meat, not to mention alcohol, but he had occasional urticaria just the same. When he came to New York he was free from symptoms. He has been here for two and one-half months. During this time he has been able to go for two weeks or ten days without having to watch his diet and then suddenly finds urticaria on his feet, arms or body. This time, however, his face and lips have not been attacked as yet. One week ago he ate pancakes and within twenty-four hours was seized with another attack of bloody diarrhea and large hives all over his body, about 0.25 cm. high, with dark red or bluish edges. Ephedrine has not relieved him at all. Now he has no diarrhea but complains of dull pain along the colon and of course intense itching of the urticaria. Examination revealed almost complete lack of the pancreatic juices. The feces show a large amount of undigested proteins. I would greatly appreciate it if you would advise me whether there is any known relation between colitis and urticaria and which is the primary cause, the colitis producing the allergic reactions or the allergy producing the colitis; whether anything is known about the role of the pancreas in allergy, whether there is any known reason for the relief obtained by old tuberculin, what could be done as far as treatment of this case is concerned and whether there is any chance of this man ever recovering from his condition.**

Kurt T. Shery, M.D., Jackson Heights, N. Y.

ANSWER.—There is no clear indication that the injections the patient received in 1931 and the subsequent local complications have any bearing on the present syndrome of urticaria and colitis. Disturbed bowel function, such as abdominal pain, discomfort, gaseous distention, spasmodic diarrhea, spastic constipation and a tender colon are frequently the result of allergic irritation of the gastrointestinal tract and are thus rather frequent accompanying symptoms in urticaria. Blood in the stools is less frequent but does occur. It is likely, therefore, that one is dealing here with an allergy involving both the skin and the bowel. The acute reaction described after eating pancakes should make one particularly suspicious of buckwheat as a possible allergen. However, there is also a possibility that the bowel dysfunction is responsible for the urticaria. This may be due to one of several reasons. An inflamed bowel may result in an increased permeability of its wall with the easier entrance of the food allergen into the circulation. An intestinal infection or an abnormal bacterial content may presumably be responsible for an allergic substance arising directly from the bacteria or from the products of bacterial action on food residues. It should also be kept in mind that the bowel disturbance may be a symptom of parasitic infestation and that the latter may be the cause of a remote urticarial allergy.

The role of the pancreas in the mechanism of allergy is not settled. There is common belief that foods are apt to cause less allergy if they are well digested, and pancreatic enzymes as well as hydrochloric acid, pepsin and bile salts have been suggested as therapeutic measures. A theory has also been presented (Oelgetz, A. W.; Oelgetz, P. A., and Wittekind, Juanita: Studies in Food Allergy: Preliminary Report, *Am. J. Digest. Dis. & Nutrition* **1**:730 [Dec.] 1934) that hypersensitiveness to food is caused by an excess of undigested food protein in the blood serum and that this excess is due to a low concentration of pancreatic enzyme in the serum. The latter, in turn, is due to an insufficient pancreatic enzyme mixing with the food in the intestinal tract. The weakness of these "absorption" theories is that it has been shown that proteins in their normal antigenic state are absorbed from the gastrointestinal tract and that in the allergic individual such absorption is not increased. As a matter of fact, for reasons not entirely clear, this absorption tends to be diminished in the allergic person.

The employment of old tuberculin in allergic conditions is based on the theory that the use of a specific allergen to which a person is sensitive creates a certain amount of resistance to other allergens. Since tuberculin allergy is common it is but natural to proceed to that type of allergic therapy when the allergen causing the complaint is not identifiable.

An attempt should be made to study the patient along the lines suggested. The possibility of bacterial infection or parasitic infestation should be considered by direct examination of the gastrointestinal tract and by intracutaneous tests with extracts of common parasites (Ascaris, tapeworm, pinworm and the like). Since the food tests have been unsuccessful, the scheme of a food diary record might throw some light on a possible food allergy. A leukocyte count following the ingestion of individual basic foods may enable one to determine which foods one can rely on to form a basic but restricted diet (Vaughan, W. T.: Further Studies on the Leukopenic Index in Food Allergy, *J. Allergy* **6**:78 [Nov.] 1934). If food allergy or other specific allergy cannot be ascertained, more or less nonspecific therapy will have to be tried. Histaminase may be given a trial, although the evidence at hand does not indicate much possibility of usefulness of this material. Histamine in small doses, beginning with 0.1 cc. of a 1:5,000 dilution and increasing to about 1.0 cc., by daily subcutaneous injections may produce benefit. Autohemotherapy with from 10 to 20 cc. of blood is sometimes efficacious. As already suggested, pancreatic enzyme and other digestive aids would also be worth trying. With regard to chances of recovery, one can epitomize the status of therapy of urticaria by saying that almost every case is difficult and that no case is hopeless.

TESTING FOR RADIOACTIVITY

To the Editor:—**Is there a method available to determine the amount of radioactive substances (thorium B in particular) in the blood and spinal fluid? Roeder has worked with an "electrometer" and has published his experiments in a German journal (Ztschr. f. d. ges. Neurol. u. Psychiat. 161:553, 1938). Is there an "electrometer" available in this country?**

M.D., Massachusetts.

ANSWER.—For several years the only known method for testing small amounts of radioactivity in the bodies of dial painters during life and after death was by means of electroscopes and gamma electrometers.

Two methods were originally employed to detect and estimate the radium in the body during life. First, by placing the patient before a gamma ray ionization chamber electrometer, measurements were made of the gamma radiations coming from the body, penetrating rays given off by radium C, which is a decay product of the radon retained in the body. The quantitative evaluation of radium C thus made is expressed in terms of the amount of radium required to produce it.

Secondly, radon estimations were made by collecting the expired air in the ionization chamber of an electroscope and determining the amount of radon or thoron (emanation from mesothorium) present. In old cases of radium poisoning approximately 45 per cent of the total amount of radium in the body gives rise to radon which escapes in the expired air; the subsequent decay products of this exhaled radon, excluding radium C, are, therefore, formed outside the body.

The measurement of this radon can be expressed in the amount of radium required to produce it. This test is also a check on the first method, determining whether radium, mesothorium or both are present, and in estimating the total radioactivity the sum of the two tests gives the total amount of radium present in the living body.

It was found that the methods as described were not sensitive enough for the detection of small amounts of radioactivity in former dial painters who were exposed from fifteen to twenty

years previously and who were still dying from osteogenic sarcoma. Nor were these methods reliable enough to detect radium poisoning in present dial painters, so that they could be removed from their exposure and elimination methods instigated.

Recently devised gamma ray detectors and direct reading counting rate meters, based on the principle of the Geiger counter, permit of more rapid and accurate estimations than electrometers and have replaced earlier methods in the diagnosis and estimation of radium poisoning. Highly sensitive quantum counters detect gamma radiation from 0.2 microgram of radium, whereas by the best electroscopic examinations the detection of less than 5 micrograms of radium in the living body was exceedingly difficult and often impossible.

These newer methods are fifty times more delicate than the older ones. Furthermore, by means of emanation methods even smaller amounts (almost to infinity) can be detected. Such methods are now in use in the detection of artificial radioactive elements (such as radio-iodine prepared by means of the cyclotron and used in experimental medicine as tracers) and in the identification and measurement of radioactive substances in the blood, feces, urine and the like.

Robley D. Evans, Professor of Physics at Massachusetts Institute of Technology, has originated and perfected many of these newer methods. Under a grant-in-aid from the National Cancer Institute, Professor Evans constructed a gamma ray detector, and a station for the detection of radium poisoning has been established in Newark, N. J. It is believed, however, that emanation methods are the most desirable.

MENORRHAGIA AND METRORRHAGIA

To the Editor:—**A white woman aged 21, a virgin, has had irregularity in the menstrual periods ever since the onset of the menses, which occurred at 13 years of age. At times a menstrual period may not occur for three or four months, while at other times a period, when it does occur, may last from three to four weeks. The patient states that two and one half years ago one period lasted five weeks, two pads a day being necessary up to the time of the cessation of the flow. She came to see me Jan. 2, 1940, with a similar complaint. Her period began Nov. 21, 1939, and she has had vaginal bleeding since. Physical examination revealed an increased amount of hair on the arms and legs and a male distribution of the pubic hair. The blood pressure was 120 systolic, 80 diastolic. Nothing was palpated in the pelvis on rectal examination. The hemoglobin was 60 per cent (Sahli). I am interested in a diagnosis in this case. I can think of a few conditions which might be etiologic factors: 1. Hypothyroidism, though the clinical picture does not resemble this condition. The patient is of average height and weight for her age, does not fatigue easily, perspires freely and has a good appetite. Unfortunately the basal metabolic rate has not been determined as yet because I feel that the patient's anemia would distort the result. 2. An adrenal cortical tumor because of the hypertrichosis. However, the patient has no hypertension and I believe that such tumors result in either complete amenorrhea or oligomenorrhea. 3. Increased estrogenic hormone secretion. I have thought that this might be a causal factor because of increased follicles in the ovary. I have not, however, as yet had a quantitative urine estrogenic hormone determination. 4. Insufficient gonadotropic secretion of the pituitary gland, resulting in inadequate control of the menses by inadequate stimulation of the ovaries. I would appreciate any information that would help toward arriving at an accurate diagnosis and any aids in therapy which would result in regularity of the menses. The flow finally ceased two days ago after treatment with iron, calcium, ergot and bed rest. The patient is a school teacher and such bouts of menstrual bleeding are incapacitating, requiring her to lose time from her work. Might a course of anterior pituitary-like hormone be tried fourteen days or so before the supposed onset of the menses? Might small doses of desiccated thyroid be of help, though the symptom picture does not resemble hypothyroidism?** M.D., New York.

ANSWER.—The menstrual irregularity of this patient does not appear to be the result of a general endocrine disturbance but seems to arise in an ovarian dysfunction alone. Endometrial biopsies are desirable in order to try to make a more definite diagnosis. Excessive bleeding due to hypothyroidism would respond satisfactorily to thyroid therapy. One or more basal metabolic tests should be made on the patient in order to prove or disprove the diagnosis of hypothyroidism. It is questionable whether thyroid therapy is of value in cases in which there is not a low basal rate or other signs of hypothyroidism. The anemia demonstrated by this patient will not interfere much with the basal metabolic studies.

Chorionic gonadotropic (formerly called "anterior pituitary-like") substance is said to control bleeding of the menorrhagia type. There is some question as to whether women in the child-bearing age respond as favorably as those near the menopause. The doses usually used are from 300 to 400 rat units hypodermically two or three times a week for one or two months. Administration of testosterone propionate has been used successfully to control menorrhagia and metrorrhagia. The doses usually administered are 10 to 25 mg. hypodermically two or three times weekly for about a month. This therapy is still experimental.

An attempt should certainly be made to overcome the anemia, stimulate red blood cell formation and build up the patient as regards her nutrition. If the patient does not bleed profusely or too long a time, there is little need for concern as regards the irregularity of the menses. After marriage, however, if the patient is sterile and desires children, attempts can be made to regulate the cycle.

ARTIFICIAL MENOPAUSE AND ESTROGENIC THERAPY

To the Editor:—**A woman aged 29 has had six children and one year ago a hysterectomy was performed. Since the operation she has complained of severe headaches, dizziness and extreme weakness. I do not know why the hysterectomy was performed but apparently it was done for subinvolution. Her general physical examination is entirely negative including an ophthalmoscopic examination and the proper fitting of glasses. She was started on theelin about one year ago when I first saw her. At first she had 2,000 unit doses three times a week with no improvement. Later the dose was increased to 10,000 units. For a while she felt better on this regimen but lately she has become much worse. 1. What are the symptoms of overdosage with estrogenic substance? 2. If the ovaries are left in at the time of hysterectomy will they function normally throughout the sexual life of the patient or do they soon undergo change?** M.D., Michigan.

ANSWER.—Presumably the reason the patient is not being relieved of her headaches, dizziness and extreme weakness is that she is not receiving large enough doses of estrogen. She may be given 50,000 international units of estrogen hypodermically once a week for three weeks and then 10,000 international units once a week for three or four more weeks. Following this or concurrently with it, the patient may take 2,000 or 4,000 international units of estrogen by mouth. She will have to increase this dose if the symptoms are not relieved and contrariwise she should take medication only once every second day if she is relieved. After a few weeks the patient can usually work out a satisfactory dosage for herself. Estrogenic therapy might have to be continued for a long time. It is assumed, of course, that a thorough examination has been made to make certain that there is no other cause for the distressing symptoms than the hysterectomy, and the matter of a possible history of cancer in the family should be considered.

1. Women can tolerate large doses of natural estrogen without disturbing constitutional signs or symptoms. Although ovarian disturbances may occur, it is conceivable however, that after prolonged administration women may develop headaches from an enlarged pituitary gland. Likewise there is the possibility that mammary or uterine carcinoma may be favored.

2. There is no unity of opinion on this subject. It is generally believed that the ovaries do continue to function after the uterus is removed. However, many gynecologists hold that this is not so; hence they remove both ovaries whenever they perform a hysterectomy. There seems to be no doubt that far fewer women have distressing menopausal symptoms following hysterectomy alone than after hysterectomy and bilateral oophorectomy. Furthermore, many women who have a simple hysterectomy do not have a change of life until a number of years after the hysterectomy.

SALT AND CARBOHYDRATES IN HEADACHE

To the Editor:—**Has there been any research on the use of sodium chloride in the treatment of migraine or "sick headache?" I am not subject to frequent headaches but when I do have one it is severe. Recently when one started I felt too nauseated to take any anodyne but had a craving for salty potato chips. I thought it could do no permanent damage to try some. The relief was immediate and dramatic. The questions in my mind are these: Could the anion of the sodium chloride be responsible for the relaxation of the smooth muscle? (I understand there is a pylorospasm.) Could this medication be of therapeutic value? Was it a coincidence? Having been called to treat so many cases of "nervous headaches," one is apt to grasp at a straw.** M.D., California.

ANSWER.—There have been as many different treatments for migraine as there have been theories regarding its etiology. It seems probable that the syndrome has different causes in different individuals, and that the success of a particular treatment varies accordingly.

Villey and Buvat (*Paris méd.* **1**:189 [Feb. 27] 1937) reported relief of migraine in three cases following the intravenous injection of 20 cc. of a 10 per cent sodium chloride solution. They attributed their results to the alleviation of cerebral edema. On the other hand, Gerson (*Wien. Klin. Wchnschr.* **45**:744 [June 10] 1932) previously claimed favorable results in decreasing the incidence and severity of attacks from the use of his diets which were low in salt content.

If there was indeed a cause and effect relationship between eating the potato chips and the relief of headache in this case, the result might also have been due to the carbohydrate content of the potatoes. Here again, the literature is contradictory.

Gray and Burtness (*Endocrinology* **19**:549 [Sept.-Oct.] 1935) reported that in certain cases of migraine the attacks coincided with periods of relative hypoglycemia and were successfully treated by frequent carbohydrate feedings. But there are, on the contrary, a number of reports (e. g. Wagner-Jauregg: *Wien. med. Wchnschr.* **85**:1, 1935; Porges: *Med. Klin.* **33**:664 [May 14] 1937) purporting to show that a low carbohydrate diet exerts a beneficial influence over extended periods of observation.

SLIGHT GENERALIZED EDEMA

To the Editor:—A married woman aged 34 has acquired a mild but persistent generalized edema. It was noticed in the feet and ankles some two months before it was present in the face, eyelids, arms and breasts, which began about Nov. 1, 1939. She describes the skin as feeling "thicker" all over and feels that the appearance of her face has changed. For the past few weeks, however, the edema has become less in the face again and more in the legs. She feels that the left leg swells slightly more than the right and has noticed that the veins behind the left knee have enlarged during this time (confirmed by examination). Except for the unpleasant swelling of her skin, the patient admits only that she is not quite as strong as previously and that she feels slightly feverish at times. She is able to continue her regular duties as a housewife with two children to take care of. She has never been pregnant, the children being her husband's by a former marriage. Her past history is uneventful except for an attack of sinusitis (of the left antrum) fifteen years ago with a recurrence though of a mild nature, which subsided rapidly without treatment about the middle of October 1939. The patient is a woman of normal appearance weighing 125 pounds (57 Kg.). Examination, which included transillumination of the sinuses, was negative except for a slight systolic blowing murmur, a somewhat eroded cervix, a moderately retrocessed uterus and slight but definite pitting edema of the ankles and legs. The swelling of the skin of the face, arms and breasts was not so definite but the feeling of abnormal thickness to the skin was insisted on by the patient. (She is a former registered nurse and there is no trace of neuroticism.) The temperature 99.4 F (by mouth), pulse 72, blood pressure 114/66, basal metabolic rate plus two, urine normal as to albumin, sugar, concentration and microscopic examination on several occasions, blood protein content: albumin 4.5, globulin 2.25, total proteins, 7.25, sedimentation time 11.5 mm. in one hour (Cutler tube), hemoglobin 75 per cent (Sahli); white count 4,200, with an essentially normal differential count. I have tried the following treatments to no avail whatever; diluted hydrochloric acid, salt poor diet, high vitamin diet and desiccated thyroid tablets, 1½ grain (0.1 Gm.) daily for ten days. I do not see how a mild infection such as suggested by the slight increase in sedimentation time and the slight fever could cause such edema even if it could be located. Can you throw any light on this perplexing case for me? I should greatly appreciate any leads you might suggest and would hasten to follow them up.

M.D., New York.

ANSWER.—The usual systemic causes of edema seem to be rather clearly ruled out in this case. A cardiac, renal or metabolic edema would not fit the physical and laboratory observations. The physical examination reveals a slight pitting edema of the lower extremities. Such a condition could be the result of local causes, either obstruction to the return circulation or venous incompetence. The combination of fever, increased sedimentation rate and leg edema suggests a pelvic infection. It is possible, although highly improbable, that an abdominal Hodgkin's disease might present this picture. Such a diagnosis would assume that some enlarged glands within the abdomen cause pressure on the return circulation.

None of these, however, would cause generalized edema in the case described. It would seem best to reserve judgment about the generalized edema until it had been personally observed.

ESTROGENIC HORMONES AND URTICARIA

To the Editor:—I am treating a white woman, aged 51, for menopausal distress with estrogenic hormones and am having some difficulty with urticarial eruptions following treatments. The patient states that she used to have eczema some years ago. I have given her estrogens biweekly at first, and lately only once a week. I have tried different preparations, all with the same result. She is greatly improved as regards the menopausal symptoms, but I am forced to discontinue therapy because of the undesirable side action. Can you tell me if this has been observed by other physicians and if there is some way to treat this patient and avoid the ill effects? Would oral preparations be apt to produce the same ill effects?

M.D., Minnesota.

ANSWER.—It is quite possible that the patient is not sensitive to the estrogenic hormone but is sensitive to the vehicle employed as a solvent, in this case the particular oil plus the preservative used in the solution, if any.

The question is asked "Would oral preparations be apt to produce the same ill effects." Oral preparations, if they do not contain the substance to which the patient is sensitive, should not cause any difficulty, provided the patient is not sensitive to estrogenic substance. That the patient is sensitive to an estrogen is possible but improbable and can easily be determined by the methods described.

SENSITIVITY TO WOOL FAT

To the Editor:—I have received an inquiry as to the frequency with which lanolin produces skin rashes. My own impression is that lanolin is about as bland a substance as can be applied to the skin. I have never heard of any one who was allergic to it. Are there any available statistics on the subject?

Norman P. Rindge, M.D., Clinton, Conn.

ANSWER.—There are few reports in the literature of sensitization to wool fat. The only ones found in the American literature are those by M. A. Ramirez and J. J. Eller (The Patch Test in Contact Dermatitis [Dermatitis Venenata], *J. Allergy* **1**:489 [Jan.] 1930) and by M. B. Sulzberger and J. L. Morse (Hypersensitiveness to Wool Fat, THE JOURNAL, June 20, 1931, p. 2099). Each paper reports two cases, all of them with positive patch tests to wool fat. One of the patients of Sulzberger and Morse was a wool salesman in whom the patch test to wool was weakly positive. The other patient, a dress designer, had a negative patch test to wool. Both gave no reaction to scratch tests. This paucity of reports of sensitivity to wool fat does not indicate that it is an uncommon phenomenon but that it is not considered remarkable enough to warrant reporting. Dermatologists see it not infrequently. Sézary remarks that it is seen oftener than sensitization to petrolatum (Intolerance cutanée à la lanoline, *Presse méd.* **44**:1880 [Nov. 18] 1936).

PAPULAR LESION IN CHICKEN FEATHER PICKERS

To the Editor:—I am plant physician to a chicken dressing factory. During the last month I have seen about fifteen girls with large numbers of warts mostly on the palmar surface of their hands. All of these girls have been feather pickers and pin feather pickers. The lesion starts as a deep pin point papule; this breaks down, discharging serous material, and then over a period of a few weeks a tender wart forms. Although irritation seems to play a big part, a few of the girls have warts on the dorsal surface of their fingers and one of them on her knee, on which there seems to be no source of irritation. The chickens have already been dipped in boiling water and molten wax for ten seconds, which would seem to suffice for superficial sterilization. Besides avoiding irritation, what would you advise for treatment and prevention? The water used at the plant has significant amounts of iron and sulfur in it. Would this influence the picture?

S. M. Berger, M.D., Selbyville, Del.

ANSWER.—The warts noted on these girls are no doubt the result of a foreign body reaction resulting from the embedding of particles of feathers, e. g. quill, shaft, pith, barbs or vane, which penetrate into the epithelial layers and produce a wart at the site. Lesions of similar type have been described in asbestos workers by A. P. Dewirtz (*Arch. f. Dermat. u. Syph.* **161**:1, 1930). He describes the occurrence on the inner surface of the hands, more often the right, of from three to five and occasionally more efflorescences which morphologically resemble a noninflammatory papule. Some are round, others angular with a rough surface, and they are usually situated in the epidermis at a point that corresponds to the penetration point of an asbestos needle in the skin. This disease has a definite localization on the palm and closely simulates the ordinary warts seen in workers in asbestos pits and is rare in other sections. The disease is produced through the penetration of the asbestos crystals into the epithelial layers. At the site of the layer there appears an extensive proliferation of cellular elements with the development of giant cells and marked cornification, and as a reaction there develop in the underlying tissue the signs of a chronic inflammatory process.

For prevention, the best approach would be to have the workers wear sturdy gloves made of rubber or one of the newer elastic fabrics. Soluble iron or sulfur in the water would not act as foreign bodies or be likely to influence the picture.

VITAMIN E

To the Editor:—Is vitamin E in large or small doses safe to administer to patients for a long period of time? I was informed that in experiments on rodents large doses predisposed to cancer. It has been suggested in lateral spinal sclerosis, also in the third stage of tabes. In both of these I question its value.

A. G. Sage, M.D., Buffalo.

ANSWER.—Four or five laboratories have endeavored without success to confirm the claim originally made by Rowntree that the feeding of crude wheat germ oil produced cancer in rats. Crude wheat germ oil, a purified product, and concentrates of vitamin E were alike ineffective either in producing cancerous lesions or in modifying their progress. Transplants of mammary carcinoma have been maintained for two and a half years in vitamin E-deficient animals without change in the cytologic character of the growth. Vitamin E thus has no effect on cancer so far as known.

The value of vitamin E in lateral spinal sclerosis remains uncertain. The dystrophy produced in experimental animals

seems to be primarily muscular in origin, and the alterations which have been described in the central nervous system have not been duplicated or confirmed. Accurately controlled clinical experience is greatly needed.

ALCOHOLIC LIQUORS WITH SULFANILAMIDE

To the Editor:—It has long been a question as to whether alcohol in the form of whisky and wines should be taken at the same time at which sulfanilamide products are being administered. Any information that you can give concerning this subject will be appreciated.

Herman C. Quantz, M.D., Bunkie, La.

ANSWER.—Ordinarily, alcohol in the form of whisky and wines should not be administered to patients who are receiving sulfanilamide or its derivatives. It has been observed that two cocktails consumed at a time when the blood concentration of sulfanilamide was 5 mg. per hundred cubic centimeters notably increased the dizziness resulting from the sulfanilamide. In general, alcohol increases symptoms of dizziness, nausea and vomiting, and the inability to coordinate that are frequently seen in the course of sulfanilamide therapy. However, in a seriously ill chronic alcoholic addict whisky would not necessarily be contraindicated because its withdrawal might result in the appearance of delirium tremens or some other form of alcoholic psychosis.

TINTED LENSES FOR MOTION PICTURE OPERATOR

To the Editor:—One of my patients who is a movie operator and is constantly looking at the pictures tells me that a tinted lens such as Crookes A or B saves him considerable eyestrain. He thinks the light is similar to sharp sunlight on the eyes, the tinted lens preventing the rays from striking the eye. Is this true? I have not been able to find any information on this point in any textbook.

David Glass, M.D., Louisville, Ky.

ANSWER.—The amount of light reflected from the screen in a motion picture house is so infinitesimal as to be negligible in the production of symptoms. However, the operator may be exposed to light from the high intensity source of illumination that is used in projecting lenses. If that is the case a tinted lens will undoubtedly give him the comfort he describes.

DIABETES AND KNOT GRASS

To the Editor:—A patient claims that the use of a certain grass has been effective in controlling his diabetic condition. He claims that it is an old European treatment. He has had this grass examined by a botanist, who identified it as knot grass, Polygonum aviculare, a member of the buckwheat family. Is there any scientific or clinical evidence to corroborate his claim?

M.D., New Jersey.

ANSWER.—From time to time one hears or reads reports of success in treating diabetes with herbs, plants or vegetables or extracts of these. Those which have been subjected to well controlled laboratory and clinical trial have not been found helpful. Although work regarding the effect of Polygonum aviculare has not been found, it seems safe to assume that this grass would likewise be valueless. It is true that the use of green leafy plants which make acceptable articles in the diet may exert a beneficial effect on patients with mild diabetes because they provide a bulky diet low in calories, but no specific value can be claimed.

NASAL PLASTIC OPERATION AND LIBIDO

To the Editor:—Several of my gynecologic patients who have undergone nasal plastic operations have stated that there has been a definite change in their libido since the operation: a few diminished, more increased. In view of the ancient belief of so-called genital spots on the tuberculum septi and inferior turbinates, might one assume that the operation produced a new nasogenital-sexual relationship? Are there any published reports by plastic or oral surgeons of a large number of cases showing changes in the libido following nasal operations? I do not, of course, refer to the increased attractiveness to the opposite sex engendered by the operation but to actual personal libidinous alterations.

Melvyn Berlind, M.D., Brooklyn.

ANSWER.—There is no anatomic reason for either an increase or a decrease in libido following nasal plastic operations, chiefly because plastic operations on the nose do not involve the tuberculum septi and inferior turbinates. There is, of course, a definite change in personality in most single girls and married women whose noses are beautified by nasal operations. Most such young women feel that they are much more attractive after they have the operation. As far as is known there has not been any published report on the relationship of nasal plastic operations to libido.

POSTPARTUM PSYCHOSES

To the Editor:—Three years ago I delivered a patient who developed a puerperal psychosis about ten days post partum. She had a rather prolonged labor because of an occiput posterior presentation. The delivery was normal. A week post partum she began to talk a lot and write lengthy letters. When she went home, fourteen days post partum, she became nervous and noisy and it became necessary to institutionalize her for a short while. She recovered completely. She remained stout and nervous. Recently she became pregnant again. What can be done to prevent the recurrence of the puerperal psychosis?

M.D., Missouri.

ANSWER.—Postpartum and postoperative psychoses constitute a heterogeneous group consisting of delirious reactions. The patient's entire medical and psychologic situation must be investigated, especially for factors of fear. Postpartum infection or absorption of toxic material are additional etiologic factors. Should this patient have a severe recurrence of puerperal psychosis the question of preventing subsequent pregnancies by contraceptive methods will have to be considered. General physical and mental hygienic measures are the only known prophylaxis, aside from preventing conception in persons subject to recurring postpartum psychosis.

ANKLE CLONUS AND BABINSKI SIGN

To the Editor:—What is the physiologic reflex mechanism involved in (1) a sustained ankle clonus and (2) an unsustained ankle clonus? A patient had tuberculous spondylitis (Pott's disease) with fairly severe kyphos in the low dorsal area and developed a spastic diplegia of both lower extremities. On bed rest and following spine fusion she has regained full use of both lower extremities for more than one year now. For the past few weeks she has been ambulatory and has no complaints. However, on physical examination she has slightly hyperactive deep reflexes in both lower extremities with unsustained but definite ankle clonus on the left. Exploratory operation revealed the spine fusion to be solid its entire length and x-ray examination shows the fusion to be long enough to splint the diseased spine. The Babinski sign is absent bilaterally. In view of these observations does the persistent ankle clonus have any prognostic significance? If the Babinski sign was positive bilaterally but ankle clonus absent in a similar case in which recovery from a diplegia due to Pott's disease was occurring (I have such a case) would there be any difference in the prognosis? In a case of upper motor neuron paralysis does ankle clonus have any significance more than the hyperactive deep reflexes convey? If so, what?

Keith E. Haines, M.D., Staten Island, N. Y.

ANSWER.—An ankle clonus means a defect in the motor pathways. This is true with both the sustained and unsustained varieties. It has practically the same significance as deep reflexes and a positive Babinski sign, though they are not necessarily concomitant. The Babinski sign indicates a more profound disturbance. The ankle clonus means slightly more than hyperactive reflexes but is on the same order.

TREATMENT OF CONGENITAL SYPHILIS IN PREGNANCY

To the Editor:—How much treatment should a congenital syphilitic patient have in a second and succeeding pregnancies and when should it be started? The positive Wassermann reaction was discovered accidentally. The patient has never had symptoms of the disease. She has received twenty injections of neoarsphenamine and sixty injections of a bismuth compound. The first baby is normal. The mother's Wassermann reaction is always positive.

M.D., Oregon.

ANSWER.—If it is established that the mother has congenital syphilis, it would be one of the really rare occurrences in the biologic course of the disease for her to be able to transmit her infection to a child even though she had never been treated for it. The treatment described is probably adequate for all eventualities, including protection of the mother against any possible recurring active manifestations of her congenital syphilis. Again, provided it is established that the mother is congenitally syphilitic, no further treatment during subsequent pregnancies is advised.

DYEING WHITE HAIR

To the Editor:—This inquiry is not strictly medical but no information can be obtained from beauty parlors or barber shops. I have a client who is only middle aged but has white hair. His face is unlined and his manner vigorous, but since he lost his job two years ago he has had difficulty in getting a job because of his white hair. He is set down as an "old man." Anything he would use to darken his hair would obviously have to be kept up indefinitely. Any suggestions would be appreciated.

Paul R. Howard, M.D., El Dorado, Ark.

ANSWER.—The necessity of dyeing hair in order to get a job is a reflection on the intelligence of employers; but if the man is convinced that dyeing his hair will help him he should have patch tests done before the dye is applied with each dye used. This test should be repeated before each retouching to guard against the possibility of sensitization to the dye acquired during the interval. In this way he will be fairly well, though not absolutely, protected against a dermatitis. According to the

new Federal Food, Drug and Cosmetic Act, dyes of this sort should be labeled "Caution. This product contains ingredients which may cause skin eruptions on certain individuals and a preliminary test . . . (sec. 601a).

SULFAPYRIDINE FOR BACILLARY INFECTIONS

To the Editor:—Will you kindly send me any information that you might have regarding the use of any specific derivatives of sulfanilamide in therapy of any infectious diseases caused by bacilli? M.D., Connecticut.

ANSWER.—Sulfapyridine and azosulfamide (neoprontosil) are the only two drugs on the American market other than sulfanilamide which have been used in the therapy of diseases caused by bacilli. There is but little evidence available regarding the efficacy of azosulfamide in bacillary infections. Sulfapyridine has been used in the treatment of Friedländer's bacillary infections, brucellosis, typhoid, Endamoeba coli infections, especially those of tissues and in the urinary tract, and in Proteus, Bacillus pyocyaneus and other bacillary infections of the urinary tract. The value of sulfapyridine in the treatment of bacillary infections has not been established and at the present time the use of this drug in such infections must be considered as still in the experimental stage.

PRESCRIPTION FOR GLASSES

To the Editor:—Refraction of the right eye when not fatigued gave nearly perfect vision with $-0.50 \times 180°$. After homatropine with paredrine it gave nearly perfect vision with $+0.50 \times 90°$. The lens prescribed was $-0.25 \times 180°$, $+0.25 \times 90°$. It gave 20/15 vision and no apparent strain. Please criticize the prescription. Is it the exact optical equivalent of -0.25 sphere, $+0.50 \times 90°$? Is either preferable? M.D., Ohio.

ANSWER.—The prescription given is the equivalent of -0.25 sphere: $+0.50c90$, which is what one would ordinarily prescribe from the retinoscopic observations as given. In writing prescriptions, the effect of the crossed cylinder is usually written in the prescriptions as a combination of sphere with the total cylinder, as -0.25 sphere: $+0.50c90$.

NIGHTMARES AND SLEEPWALKING

To the Editor:—The mother of a 12 year old boy who "has nightmares and walks in his sleep" inquires whether there is any help for this condition. Reference books at hand do not give me any help in answering her inquiry. Do you know of any useful advice that I can give her?

M.D., California.

ANSWER.—It is important in such cases to be sure first that petit mal is not present and second that the gastrointestinal tract has normal function. It is advised that no food be given for three hours before bedtime and that three-fourths grain (0.05 Gm.) of pentobarbital sodium be given one-half hour before bedtime. Light bedclothes and good ventilation are important during sleep.

AIR IN TISSUES

To the Editor:—In connection with the inquiry regarding absorption of air by tissues (The Journal, February 24, p. 680), I report a personal incident. In a carriage runaway I was thrown out, the carriage was tipped over on top of me and I was dragged some yards with the hub cap of the carriage wheel against the lateral surface of my right leg, just above the knee. This resulted in a deep, semicircular laceration which penetrated the skin and fascial planes down into the deeper muscular tissues. Three hours later, following ordinary treatment which consisted of washing out this wound and others with soap and hot water and applying iodine freely, plus sterile gauze dressings (also antitetanus injections), I noted a distinct area of swelling of the thigh, with pronounced crackling sounds when touched by the fingers and expulsion of air from the lacerated wound. This area extended along the lateral surface of the thigh from the knee joint upward approximately 12 inches and was from 3 to 5 inches wide. Being entirely alone, without professional consultants of experience, I naturally thought of "gas gangrene" and that night when two capable surgeons happened to be passing through I eagerly called them in for advice. Fortunately the extent of the area had not increased (I had marked it on the surface), but they both felt that liberal incisions to release the "gas" were called for. However, it was my leg, and I did not feel that gas could develop so rapidly and so temporized until the next morning. During the night I could feel and hear the escape of air from time to time through the laceration, and by morning the area of crackling had decreased nearly 50 per cent, but it was not until forty-eight hours after the original wound that all the air had passed out. I could feel that the air was not only subcutaneous but in the deeper muscular tissues as well, owing probably to the twisting, circular action of the hub of the wheel, which had loosened the various deeper structures and allowed air to pass in. Without any treatment other than occasional changing of the dressing, the unsutured would healed by first intention in eight days. There was, of course, no way of measuring the actual amount of air that had penetrated into the tissues, but from the area involved and the amount that actually passed out of the tissues, I would estimate that between 200 and 300 cc. of air had entered.

Hartman A. Lichtwardt, M.D.,
American Hospital, Hamadan, Iran.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, June 29, page 2588.

STATE AND TERRITORIAL BOARDS

ALASKA: Juneau, Sept. 3. Sec., Dr. W. W. Council, Box 561, Juneau.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, July 15. *Written examination.* Los Angeles, July 15-18. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

CONNECTICUT: *Written.* Hartford, July 9-10. *Endorsement.* Hartford, July 23. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homeopathic.* Derby, July 9-10. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination.* Dover, July 9-11. *Reciprocity.* Dover, July 16. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, Oct. 21-22. Sec., Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: *Basic Science.* Gainesville, Nov. 1. *Applications must be on file not later than Sept. 16.* Sec., Dr. John F. Conn, John B. Stetson University, De Land.

IDAHO: Boise, Oct. 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Oct. 1-3. Superintendent of Registration, Mr. Lucien A. File, Springfield.

IOWA: *Basic Science.* Des Moines, July 9. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MASSACHUSETTS: Boston, July 9-11. Sec., Dr. Stephen Rushmore, 413-F State House, Boston.

MONTANA: *Reciprocity.* Helena, Sept. 30. *Written.* Helena, Oct. 1-2. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science.* Lincoln, Oct. 1-2. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

NEVADA: *Reciprocity with oral examination.* Aug. 5. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW MEXICO: Santa Fe, Oct. 7-8. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

OREGON: *Basic Science.* Portland, Oct. 26. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: *Written.* Philadelphia and Pittsburgh, July 9-11. *Bedside.* Philadelphia, July 12-13. Dir., Bureau of Professional Licensing, Dr. James A. Newpher, 358 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, Sept. 3. Sec., Dr. O. Costa Mandry, Box 3854, Santurce.

RHODE ISLAND: Providence, July 10-11. Sec., Division of Examination, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Rapid City, July 16-17. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

WASHINGTON: *Basic Science.* Seattle, July 11-12. *Medical.* Seattle, July 15-17. Sec., Department of Licenses, Mr. Nelson N. Vaughen, Olympia.

Colorado April Examination

Dr. Harvey W. Snyder, secretary, Colorado State Board of Medical Examiners, reports the written examination held at Denver, April 3-5, 1940. The examination covered eight subjects and included sixty-eight questions. An average of 75 per cent was required to pass. One candidate was examined and passed. One physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Illinois College of Medicine		(1936)	88.2

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Nebraska College of Medicine		(1936)	N. B. M. Ex.

Ohio Reciprocity Report

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports twenty physicians licensed by reciprocity and two physicians licensed by endorsement on April 2, 1940. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Indiana University School of Medicine		(1920)	Indiana
State University of Iowa College of Medicine		(1936)	Iowa
University of Louisville School of Medicine		(1935), (1939, 2)	Kentucky
University of Michigan Medical School		(1931)	Michigan
Wayne University College of Medicine		(1939)	Michigan
St. Louis University School of Medicine		(1937, 2), (1938, 2), (1939, 2)	Missouri
Washington University School of Medicine		(1934)	Missouri

University of Nebraska College of Medicine	(1938)	Nebraska
New York University College of Medicine	(1931)	New York
University of Toronto Faculty of Medicine	(1936)	Michigan
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest	(1911)	New York
Université de Genève Faculté de Médecine	(1935)	Maine, New York

LICENSED BY ENDORSEMENT

School	Year Grad.	Endorsement of
Yale University School of Medicine	(1936)	N. B. M. Ex.
Boston University School of Medicine	(1937)	N. B. M. Ex.

Book Notices

Blood Transfusion. By Victor Horsley Riddell, M.D., F.R.C.S., Assistant Surgeon and Lecturer in Operative Surgery, St. George's Hospital, London. Cloth. Price, $6. Pp. 370, with 65 illustrations. New York & London: Oxford University Press, 1939.

Here is an authoritative and thoroughly practical treatise on the practice of blood transfusion. While much has been written on this important subject, few sources of information will yield such a wealth of workable facts as this volume. The book reflects the author's intimate familiarity not only with the descriptive aspects of the subject but with practice as well. The material is particularly well organized and adequately illustrated. It is concisely presented without sacrificing clarity. All material extraneous to the practical phases of the subject has been purposely omitted. Although the author is English, he has traveled extensively in the United States and Canada and has managed to include the best practice current in this country as well as abroad. The material is distinctly cosmopolitan and carefully chosen. Technical details are explicitly given in a minimum amount of space. Each chapter is summarized and a current and pertinent bibliography is appended. The chapters on blood grouping technic, the universal donor, physiology of the blood groups and complications of blood transfusions are particularly well done. Few sources of information will yield as much fact in such a small space. The indications and contraindications to blood transfusion are clearly drawn and outlined. The information is direct and authoritative. The relative therapeutic values of whole and of citrated blood are discussed together with explicit directions for their use. The author candidly states that no reasonable or convincing evidence exists for therapeutic priority of either. Facts are dispassionately presented for each method. The chapter on apparatus is excellent and should prove invaluable to the physician as well as institutions. The chapter on stored blood embodies such experiences as the blood banks at the Cook County Hospital and at the Soviet blood transfusion institutes, and the use of cadaveric blood and placental blood. Limitations and virtues are discussed. The organization of a transfusion service and the subject of voluntary and professional donors are considered. This book deserves a place in every hospital and library. It is a working manual on the practice of blood transfusion pregnant with useful data and instruction. For a current comprehensive but concise treatise on this subject this textbook is preeminent. Every physician can purchase the volume with conviction that he has added something concrete to his working knowledge of medical practice.

Combined Textbook of Obstetrics and Gynæcology for Students and Medical Practitioners. Revised and Rewritten by J. M. Munro Kerr, LL.D., M.D., F.R.F.P. & S., et al. Third edition. Cloth. Price, $12. Pp. 1,192, with 499 illustrations. Baltimore: William Wood & Company, 1939.

The attempt of the nine authors to cover the subjects of obstetrics and gynecology in a single volume has been fairly well accomplished. It is natural, however, that a few subjects should receive scanty space. This is particularly true of operative gynecology and endocrinology. Only a total of thirteen pages is devoted to the three subjects "Ovulation and the Functions of the Ovary," "The Other Endocrine Glands" and "The Menopause." Surely in a book on obstetrics and gynecology containing a thousand pages more than thirteen should be devoted to the endocrine glands. The authors frequently refer to the use of intra-uterine douching, particularly for the removal of débris after an abortion and for stimulating uterine contractions during postpartum hemorrhage. In the United States few obstetricians employ intra-uterine douches for any purpose. The authors believe that version (not followed by extraction) is the sheet anchor of the general practitioner faced with a grave case of placenta praevia. Nearly every patient who bleeds should be sent to a hospital, where far more satisfactory methods of treatment may be employed. Version through an incompletely dilated cervix in the presence of hemorrhage is a formidable and dangerous procedure. Even in the home the use of forceps on the baby's scalp as recommended by Willett and advocated also by the authors is far simpler and safer. For the low cervical operation the authors favor and illustrate the transverse incision in the lower uterine segment. They believe there is still a place for accouchement forcé or forcible dilation of the cervix followed by extraction of the child, especially when there is protracted labor caused by rigidity of the external os. For this purpose they mention the Bossi dilator, of which they say "Even when the greatest care is taken and the cervix very slowly stretched it is difficult to avoid doing serious injury. There is no place for this type of instrument." In spite of this statement, an illustration of the Bossi dilator is reproduced. Notwithstanding the number of men collaborating in the preparation of this book, the style is uniform throughout. The individual chapters, except two special ones, are not credited to individual authors. The illustrations are numerous and instructive but a large number were taken from other books. At least twenty-five are from Young's recent Textbook of Gynecology.

Arzt und Laboratorium: Die chemischen und mikroskopischen Untersuchungsmethoden und ihre Verwertung am Krankenbett. Von Dr. Hellmut Marx, Chefarzt der inneren Abteilung der Krankenanstalten in Bethel bei Bielefeld. Boards. Price, 6 marks. Pp. 163, with 16 illustrations. Leipzig: Georg Thieme, 1939.

The purpose of this concise treatise is to describe briefly the most important laboratory methods that are of practical value in the practice of medicine. It is not a compendium of laboratory methods and makes no pretense at covering the field. The objective of the author apparently has been to select carefully those laboratory examinations which may be of distinct value to the practitioner in his daily work. The text contains chapters on urine examinations, kidney function test, gastric juice, bile, sputum, puncture fluids, basal metabolism determinations, blood chemistry and hematology. The chapter on blood chemistry and hematology occupies nearly half of the entire text. While this book has merit as a concise and current textbook of this subject, it is below the standard of similar books published in this country.

Pathology: An Introduction to Medicine and Surgery. By J. Henry Dible, M.B., F.R.C.P., Professor of Pathology in the University of London (The British Post-Graduate Medical School), London, and Thomas B. Davie, B.A., M.D., M.R.C.P., Professor of Pathology in the University of Liverpool, Liverpool. Cloth. Price, $10. Pp. 931, with 374 illustrations. Philadelphia: Blakiston Company, 1939.

This textbook of pathology is a culmination of teaching effort in presenting the subject as "the grammar of medicine and surgery." The organization is different from many conventional works in that subdivisions into general and special pathology are not followed. Instead the first section of the book deals with inflammation, vascular disturbances, cellular damage and degenerations, disorders of growth and immunity. The succeeding section deals with special infections and anthrax, diphtheria and actinomycosis, which are discussed at some length as representative members of septicemic, toxemic and subacute inflammatory processes. Next the more common infections and virus diseases are discussed. The third section deals with systemic pathology. The arrangement of the book is distinctly peculiar to the system of pedagogy employed by the authors and is worthy of some reflection. The book is essentially a textbook written for students but can be profitably read by practitioners. The discussions are concise but adequate for an introductory course. The trend of the text is toward aiding the student to appreciate pathogenesis rather than the recognition of fixed morbid changes. The book is an excellent introduction to clinical medicine for this reason and should find favor with medical students in this country. It is written in an engaging literary style and represents a careful selection of subject material.

Anatomy and Physiology. By Frederic Theodore Jung, B.S., Ph.D., M.D., Assistant Professor of Physiology and Pharmacology, Northwestern University Medical School, Chicago, Anna Ruth Benjamin, B.A., M.D., Resident Physician, Elgin State Hospital, Elgin, Illinois, and Elizabeth Carpenter Earle, B.A., R.N., Educational Director, School of Nursing, St. Elizabeths Hospital, U. S. Department of Interior, Washington, D. C. Cloth. Price, $3.50. Pp. 637, with 342 illustrations. Philadelphia: F. A. Davis Company, 1939.

This textbook for nurses incorporates many innovations which could be profitably utilized for other groups as well. It is distinctly an original presentation both in composition and in presentation. Many of the time honored pedantries traditionally found in a work of this type are refreshingly omitted. Pertinent facts are presented in a concise and interesting manner. Correlations between structure and function are expressed in the simplest possible terms, and at the end of each topic discussion the authors relate each part to the body as a whole. The entire text is well integrated and condensed to the greatest possible brevity. The book is attractively bound and the quality of paper and print is unusual for a textbook. The illustrations are plentiful and original and many of them are in four colors. The material is easily read in the two column pages. The book is of unusually high quality in every respect and should be warmly received as a textbook of unusually high merit by the nursing profession. It is distinctly an original presentation and the authors have made a distinct contribution to nursing education.

Pathogenic Microörganisms: A Practical Manual for Students, Physicians and Health Officers. By William Hallock Park, M.D., and Anna Wessels Williams, M.D. Eleventh edition. Cloth. Price, $8. Pp. 1,056, with 260 illustrations. Philadelphia: Lea & Febiger, 1939.

This book has long been regarded as a classic on its subject and will survive as a monument to Dr. Park, who died shortly after this revision was completed. This edition has been thoroughly revised and enlarged to include a section on bacterial variation and one on the metabolism of bacteria. The sections on pathogenic yeasts and molds, pathogenic protozoa and filtrable viruses have undergone complete revision. Other chapters have likewise undergone definite changes and additions. A number of prominent workers in special fields cooperated with the author to bring the material down to date in the usual authoritative manner that has always characterized this textbook. Not only do these additions make the work a rich source of information for medical students and laboratory workers, but the stress that has been given to problems of immunity, etiology and diagnosis of infectious diseases make it indispensable as a rich source of reference for the practicing physician. Few textbooks on this subject have the active collaboration of such authorities in their respective fields as this one. The changes in the new edition have been such that medical students, laboratory workers and libraries should have it in their possession. It is unquestionably the most current, concise, authoritative one volume textbook on bacteriology in any language.

Diseases of the Mouth. By Sterling V. Mead, D.D.S., B.S., M.S. Fifth edition. Cloth. Price, $12.50. Pp. 1,059 with 696 illustrations. St. Louis: C. V. Mosby Company, 1940.

Apparently this is a popular textbook probably because of its inclusiveness, because of the liberal use of reproductions of well chosen roentgenograms, and because of the emphasis on diagnosis and treatment. It is largely limited to the field of minor oral surgery and related diseases, as reference to such matters as cleft palate, jaw resections and plastic operations is brief. Each chapter is followed by a generous bibliography. The present edition appears twelve years after the first. It and other late editions are characterized chiefly by progressive increase in size, as the defects and redundances of the early editions persist. Of the ninety microscopic illustrations only about one third are worthy of inclusion or serve a useful purpose. Of the sixty-three colored plates, twenty-five could be discarded and not be missed. The legends are inadequate, incomplete and at times confusing, as that attached to figure 268 on page 473, which after long search is found to be connected with a case history on page 466. In figure 189 a protozoologist will no doubt locate the two amebas, but that is too much to expect of the general reader. It is suggested that the so-called pulp stones shown in figure 213 may be enamel drops, that a quart or more of orange juice daily in the routine treatment of osteomyelitis or anything else is excessive and that the prognosis in agranulocytotic angina is not always bad. The text on the subject of dental caries illustrates a tendency of the author to handle a subject by the reproduction of numerous quotations from other authors without any attempt to weave them together logically by comment and discussion. This plan increases the size of the book without increasing its popularity. These serious faults detract from the advantages listed in the first sentence and greatly limit its usefulness.

Do You Want to Become a Doctor? By Morris Fishbein, M.D., Editor, Journal of the American Medical Association. Cloth. Price, $1.50. Pp. 176. New York: Frederick A. Stokes Company, 1939.

As far as the practice of medicine is concerned, much has been said and little done about vocational guidance. The boy or girl contemplating a career in medicine has, at best, consulted a friendly physician but too often, without competent advice, has plunged headlong into the preparation for one of the most difficult and exacting professions. The author of this book has made available, in readily accessible form, a great deal of the information on which such a decision should be based. The opening chapters deal with medical education, its standards, costs and specific requirements, including the internship. Then follows a discussion of licensure and state examinations. Various phases of practice are described together with the ancillary vocations of various types of technicians. The closing chapters are devoted to the future of medicine and its relationship to society. Not the least illuminating to the neophyte are the admirably selected quotations portraying the life and character of the physician. Stevenson and Dean Inge, Percival and Sir William Osler, and many others, unite in expressing those ideals which have guided the medical profession and made it what it is.

Fuss und Bein: Ihre Erkankungen und deren Behandlung: Ein Lehrbuch. Von Prof. Dr. med. Georg Hohmann, Direktor der Orthopädischen Universitäts-Klinik Frankfurt a. M. Third edition. Paper. Price, 26.70 marks. Pp. 462, with 405 illustrations. Munich: J. F. Bergmann, 1939.

The basic difference between this edition and others is the emphasis that is placed on the early recognition of abnormal and weak feet, and the recommendation of immediate treatment for the underlying mechanical condition. The author considers early treatment as part of the general education of the physiology of the body in order to prevent progression of abnormal foot conditions. In the last five years the shoe industry has made much progress. Orthopedic shoe makers are required to take special examinations and are educated scientifically from both theoretical and practical points of view. The shoe industry is cooperating with the orthopedic surgeons. The contents of the book include some excellent illustrations, line drawings and photographs. The subjects of clubfoot and deformities of the feet are omitted. The outline of the book and description of various conditions are interesting and stimulating to the orthopedic surgeon. The military point of view is emphasized. From the practical standpoint the book is helpful in diagnosis and treatment.

Surgical Applied Anatomy. By Sir Frederick Treves, Bart. Revised by Lambert Rogers, M.Sc., F.R.C.S., F.R.C.S.E., Professor of Surgery, University of Wales. Tenth edition. Fabrikoid. Price, $4.50. Pp. 748, with 192 illustrations. Philadelphia: Lea & Febiger, 1939.

This edition has been prepared by Prof. Lambert Rogers of the University of Wales. It constitutes a general revision of the ninth edition (edited by Prof. C. C. Choyce) with the addition of new material which has become available and applicable during the last five years. Mr. Rupert Parry and Mr. R. D. Owen have assisted in revision of the section on the eye, ear, nose and throat. The new material appears especially in the sections on cranial contents, on the neck and, to a less extent, in those on the orbit and eye and on the abdomen. The value of the book is sufficiently attested by its popularity for nearly sixty years. It was originally prepared by Sir Frederick Treves for students coming up for final English examinations in surgery. Students have found it an interesting and valuable indication of the clinical usefulness of anatomic facts, and practitioners have found it a valuable and reliable guide to clinical anatomy.

Rheumatism. By H. Warren Crowe, D.M., B.Ch., M.R.C.S., Senior Physician of the Charterhouse Rheumatism Clinic. Cloth. Price, 12s. 6d. Pp. 280, with 31 illustrations. London: John Bale Medical Publications Ltd., 1939.

This book was written entirely for the benefit of those who take an active part in the treatment of chronic rheumatic diseases and who are interested in the theory underlying modern technic and its practical application. The material is based on the experience of the author at the Charter House Rheumatism Clinic in London and his practice, limited entirely to rheumatic diseases. Experimental work carried out by the members of his staff has been included. The formation and progress of the Charter House Rheumatism Clinic are described. Dr. Crowe believes that all chronic rheumatic diseases are the result of the reaction of skeletal tissues to a foreign substance, the commonest of which is a bacterium of low virulence. The conclusions drawn are based on observation of more than 10,000 rheumatic cases extending over a period of thirty years. Vaccines are vigorously advocated. The chapters on roentgen therapy, orthopedic surgery, manipulation and physical therapy were written by specialists on the staff of the clinic.

Studies on Dysplastic Acetabula and Congenital Subluxation of the Hip Joint with Special Reference to the Complication of Osteo-Arthritis. By Gunnar Wiberg. Acta chirurgica Scandinavica Vol. LXXXIII, Supplementum LVIII. Paper. Pp. 135, with 52 illustrations. Stockholm: P. A. Norstedt & Söner, 1939.

This small monograph, written by one of Professor Waldenstrom's assistants, contains some interesting material on the anatomy and x-ray appearance of the normal hip. From his studies of hundreds of normal cases, the author evolved a method for determining whether the joint is normal or pathologic. He then examined many patients who had been roentgenographed during childhood so that a chronological study was possible. The author provides an elaborate description of methods of measuring to differentiate the normal from the abnormally developed acetabula. He discusses the connection between osteoarthritis with dysplastic acetabula and congenital subluxation of the hip. The section on arthrography is especially interesting.

The Life and Death Instincts (The Vita and the Fatum). By Arthur N. Foxe, M.D. Cloth. Price, $2. Pp. 64. New York: Monograph Editions, 1939.

This small pamphlet is filled with a verbalistic juggling with the abstractions of psychoanalytic instinct theory. If Freud called his instinct theory "our mythology" this pamphlet deserves the name of "supermythology." It will be difficult for the reader to distinguish any logical connection between the different chapters which deal with such a broad variety of topics as the problem of criminality (the author calls it criminosis), the essence of life and death, fate (the author introduces a new expression fatalisation), chance and determinism, war and peace, and transference of the psychoanalytic process. The one connecting link between all this is generous references to Greek mythology. The clearest part of the pamphlet is the introduction, covering two pages.

Handbook of Orthopaedic Surgery. By Alfred Rives Shands Jr., B.A., M.D., Medical Director of the Nemours Foundation, Wilmington, Delaware. In collaboration with Richard Beverly Raney, B.A., M.D., Associate in Orthopaedic Surgery, Duke University School of Medicine, Durham, North Carolina. Second edition. Cloth. Price, $4.25. Pp. 567, with 154 illustrations by Jack Bonacker Wilson. St. Louis: C. V. Mosby Company, 1940.

The first edition of this popular work, published in 1937, was well received. In the present edition there have been some definite changes. It is neater and more compact because of improvement in texture of paper, reduction in size of illustrations and deletion of unnecessary words and illustrations. There have been additions to the manuscript and illustrations in bringing the subject down to date. The illustrations, chiefly pen and ink drawings, contribute greatly to the value of the book. The bibliography, a valuable attribute of the volume, has been revised by addition of new material to July 1939. For purposes of classroom instruction there are twenty-four chapters of sound fundamental practical and theoretical orthopedic surgery. The views expressed are a combination of the best that can be obtained from the literature, textbooks and personal experience of the authors. It is unnecessary to review the subject matter because it would be merely a review of the best opinions of orthopedic surgery in its entirety. This is probably the best book written purely as a handbook for orthopedic students and will continue to be popular in that role.

Recent Advances in Neurology. By W. Russell Brain, D.M., F.R.C.P., Physician with charge of Out-Patients to the London Hospital. Fourth edition. Cloth. Price, $5. Pp. 364, with 24 illustrations. Philadelphia: Blakiston Company, 1940.

The publication of a fourth edition of this work within ten years indicates the widespread use and acceptance of this small volume. Brain assiduously has kept his editions modernized with alterations in the text and addition of new material. As a means of keeping abreast of progress in the field of organic neurology the work is excellent if used not as a textbook but as an initial point of reference.

Malyariya: Materialy k ucheniyu ob epidemiologii i patogeneze. [By] F. M. Toporkov. [Epidemiology and Pathogenesis of Malaria.] Boards. Pp. 192, with 10 illustrations. Stalingrad: Oblastnoe Knigoizdatelstvo, 1939.

This small volume is concerned principally with statistical data on the incidence of malaria in the Union of Soviet Socialist Republics. The author suggests a program for a more effective control of both the epidemic and the endemic occurrence of the disease. No new or important observations are presented.

We Grow Up. By J. L. Kaukonen, Assistant Health Education Specialist. Federal Security Agency, U. S. Public Health Service. Educational Publication No. 3. Paper. Pp. 40, with illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1940.

This pamphlet is an education publication, highly artistic in its conception and exceedingly useful in the facts that it conveys. It is a book designed to educate the young about "the facts of life."

Nursing as a Profession. By Esther Lucile Brown. Second edition. Boards. Price, 75 cents. Pp. 157. New York: Russell Sage Foundation, 1940.

This edition follows the same general pattern as its predecessor and shares its values and limitations. Added material deals with the recommendations of the Interdepartmental Committee to Coordinate Health and Welfare Activities, the report entitled "Essentials of a Good Nursing School" and the recently revised Curriculum Guide for Schools of Nursing. Reference is also made to the activities of the Committee on Accrediting of the National League of Nursing Education. The author's question "Is Nursing a Profession?" remains unanswered.

Minlivist mikrobiv i bakteriofagiya (Trudi naukovoï konferentsiï, Kiïv, 1936). [Microbe variability and Bacteriophage (Papers of the Scientific Conference, Kiev, 1936).] Paper. Price, 22krb. Pp. 488, with illustrations. Kiev: Ukr. SSR Academy of Sciences Press, 1939.

The volume is a collection of papers on the subject of microbe variability and bacteriophage presented at the scientific conference at Kiev in 1936 and published by the Academy of Sciences of Ukraine. It is a veritable encyclopedia of information on the subject.

Ten Years in the Congo. By W. E. Davis. Cloth. Price, $2.50. Pp. 301. New York: Reynal & Hitchcock, 1940.

The modern medical missionary is a scientific adventurer. When Dr. Davis went into the heart of the Belgian Congo he carried drugs, surgical tools, medical ability, human kindliness and a sense of humor. The story is therefore fascinating and should be an inspiration to the modern physician who finds the practice of medicine possible only with a retinue of assistants, technicians, hospitals and laboratories.

Zbirnik prats prisvyacheniy pamyati akademika M. F. Melnikova-Razvedenkova. Recueil de travaux dédié a mémoire de N. F. Melnikov-Razedenkov, membre de l'Académie des sciences. Paper. Price, 25 krb. Pp. 471, with illustrations. Kiev: L'Académie des sciences de la RSS d'Ukraine. 1939.

This is a memorial volume to Prof. N. F. Melnikov-Razvedenkov, a prominent neuropathologist and member of the Academy of Sciences, who died on Dec. 20, 1937. The volume consists of thirty-three papers dealing with various clinical subjects. It does not lend itself to a review for THE JOURNAL.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Fracture of Mandible Resulting from Extraction of Impacted Molar.—The defendant dentists, Bloomenthal and Bennecke, on March 24, 1934, extracted the plaintiff's lower left third molar, which was impacted. After coming out of the anesthesia the patient suffered intense pain and a grating sensation when she attempted to move her jaw. After repeated requests during the next three days defendant Bloomenthal visited the patient on March 28 and again on March 30. She told him, so she said, about the pain, the grating sensation and the difficulty she experienced in opening her mouth. From March 31 to April 3 the patient visited the defendants several times at their offices and, as she stated, although she reiterated her complaints the defendants failed to do anything other than to administer mouth washes. On her next visit, April 4, eleven days after the extraction, the defendants caused roentgenograms to be taken for the first time. These roentgenograms and others taken later showed a fracture of the left side of the patient's mandible, but the defendants told her that the roentgenograms showed only "some sloughing of the bone" and "a sequestrum." She showed the defendants a piece of bone which she had removed from her mouth but they assured her that that "was perfectly natural." They did not immobilize her jaw in any way. About ten days after the extraction a paralysis of her left jaw developed associated with drooling of saliva. As her condition did not improve, on April 19 she consulted her family dentist, Dr. Nannestad, who took a roentgenogram which indicated to him "a complete fracture of the jaw." He sent her to Dr. Schaefer, an oral surgeon, to whom for purposes of interpretation the defendants had already shown their roentgenograms. Dr. Schaefer operated on her lower jaw, curetted the site of the extracted tooth and removed therefrom a piece of dead bone. Thereafter the patient improved steadily.

The patient sued the defendants for malpractice, alleging that they, incident to an unskilful extraction, broke her lower jawbone, failed to discover promptly the fracture and failed to treat the condition for some time, which negligence resulted in infection and improper closure of the teeth. A judgment of the trial court in favor of the plaintiff was reversed by the appellate court, first district, Illinois, holding that a verdict for the dentists should have been directed because the evidence was not sufficient to justify a judgment for the plaintiff. The plaintiff then appealed to the Supreme Court of Illinois.

At the trial a Dr. Remington, an orthopedic surgeon, testified that the roentgenogram taken by Dr. Nannestad on April 19 disclosed a "complete break" of the mandible. The fracture, he believed, should have been immobilized and failure to do so could cause both a "condition of anesthesia" in the jaw and malocclusion. A roentgenologist, Dr. Zeitlin, testified that this roentgenogram showed a "comminuted or complete fracture." Dr. Bernard, an oral surgeon, could find in the roentgenogram nothing to indicate a fracture. Bennecke testified that the roentgenograms taken by the defendants, which had been destroyed by a fire shortly after the suit was instituted, showed "a little crack there in the jaw . . . no appreciable separation of the bone, or anything of that sort." He admitted, however, that the roentgenogram taken by Dr. Nannestad did show a "comminuted fracture" of the mandible and that he treated the case as one of infection. Both defendants testified that their examinations revealed no displacement, malocclusion or crepitation. Dr. Schaefer testified for the defendants that when he first examined the plaintiff, about one month after the extraction, he found no marked displacement or malocclusion and nothing to indicate a fracture, and that he never detected any crepitation. His examination of roentgenograms revealed nothing to indicate a comminuted fracture of the mandible.

The patient contended that the trial court properly denied the defendants' motions for a directed verdict in their favor because there was evidence to show that they concealed from her the fracture of her mandible and further that their failure to immobilize her jaw caused it to become malalined and paralyzed. In passing on such a motion, said the Supreme Court, the evidence must be construed most favorably to the party adverse to it. Here the evidence so construed tended to show that prior to the extraction the patient's jaw was neither malocculded nor paralyzed; that the defendants broke her lower jawbone during the extraction; that one of them, with reluctance, visited her at home; that eleven days after the extraction they took roentgenograms and, according to their own testimony, ascertained that she had a "cracked jaw" but did not so advise her; that the existence of a fracture of the mandible may be definitely determined by roentgenograms if it is completely broken through; that a roentgenogram taken April 19, before she received treatment by another dentist, disclosed a complete fracture; that the patient repeatedly told the defendants that she experienced a grating sensation when she moved her jaw; that a "cracked jaw," accompanied by a grating sensation, is indicative of a complete fracture; that the usual and accepted treatment for a complete fracture is immobilization, and that as a result of the defendants' failure to give or prescribe such treatment a permanent condition of malocclusion and paralysis of her jaw and chin developed. There was testimony, however, that the plaintiff's lower jawbone, if broken, was not a complete or comminuted fracture but merely an incomplete or partial one, and that if the latter condition existed the treatments given by the defendants were recognized as proper. Likewise, the defendants denied that the plaintiff ever complained to them about the grating sensation. On these and other factual questions the testimony was conflicting. The testimony of both defendants and of Dr. Schaefer, was, however, in accord that a "crack" in the plaintiff's mandible and a grating sensation when she opened her mouth, if those conditions were present, would indicate a complete fracture. Similarly the defendants and Dr. Remington and Dr. Schaefer agreed that a complete or comminuted fracture of the mandible would require immobilization. Regardless of the weight of the evidence, said the Supreme Court, the patient's evidence, standing alone, tended to show that the defendants did not use the skill and care in treating her after the extraction that dentists ordinarily use in similar circumstances and that she suffered permanent injury as a proximate result thereof. Accordingly, the Supreme Court held that the trial court's refusal to direct a verdict for the defendants was proper.

The Supreme Court did not agree with the defendants' contention that they had made only an erroneous diagnosis and were therefore not liable. The testimony tended to show more than a faulty diagnosis, namely, that the defendants knew that the mandible was "completely severed" but nevertheless they treated it as a "partially cracked jaw." Nor was there any question as to whether proper treatment had been given, since it was conceded that no treatment whatever was given or prescribed for a comminuted fracture.

The Supreme Court therefore reversed the judgment of the appellate court and remanded the cause to that court for further proceedings in accordance with the above opinion.—*Shutan v. Bloomenthal (Ill.), 20 N. E. (2d) 570.*

Society Proceedings

COMING MEETINGS

National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Pacific Northwest Medical Association, Spokane, Wash., July 10-13. Dr. C. W. Countryman, 407 Riverside Ave., Spokane, Wash., Secretary.

Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

Virginia, Medical Society of, White Sulphur Springs, W. Va., July 29-31. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.

West Virginia State Medical Association, White Sulphur Springs, July 29-31. Mr. Joe W. Savage, Public Library Bldg., Charleston, Executive Secretary.

Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Digestive Diseases, Huntington, Ind.

7:189-226 (May) 1940

Extrarenal Azotemia in Gastrointestinal Hemorrhage: I. General and Clinical Consideration. D. H. Kaump, Temple, Texas, and J. C. Parsons, Des Moines, Iowa.—p. 189.

Id.: II. Experimental Observations. D. H. Kaump, Temple, Texas, and J. C. Parsons, Des Moines, Iowa.—p. 191.

Maximal Acidity of Intestinal Contents During Digestion. J. E. Thomas, Philadelphia.—p. 195.

*Acidity Modification Therapy in Peptic Ulcer. F. Steigmann and B. Fantus, Chicago.—p. 197.

*Secretory Studies in Whole Stomachs: Determination of Phenol Red in Gastric Contents. F. Hollander and A. Penner, with technical assistance of M. Saltzman and J. Glickstein, New York.—p. 199.

Use of Phenol Red as Dilution Indicator in Gastric Analysis. A. Penner, F. Hollander and A. Post, New York.—p. 202.

Psychic Gastric Secretion in Man. A. L. Bloomfield, San Francisco.—p. 205.

Studies in Human Biliary Physiology: IV. Comparative Effects of Orally Administered Olive Oil, Oleic Acid and Glycerin. With and Without Bile Salts, on Quantity of Bile Secretion. I. C. Zuckerman, M. Jacobi, B. Kogut and B. Klein, Brooklyn.—p. 208.

Some Remarks on Habitual Constipation and Related Nervous Disorders of Rectum. J. Bauer, New Orleans.—p. 210.

Volvulus of Stomach. R. Schatzki and F. A. Simeone, Boston.—p. 213.

Acidity Modification Therapy in Peptic Ulcer.—Steigmann and Fantus determined the antacid properties of four substances in the treatment of 100 patients with peptic ulcer. The substances were: (1) Sippy No. 1 powder (one part of calcium carbonate to three parts of sodium bicarbonate), (2) amphojel (a representative of the colloidal aluminum hydroxide group), (3) a neutralized karaya gum (representing the mucilagenous group) and (4) acid-bismuth mixture (a mixture of bismuth subnitrate and dilute nitric acid). All four antacids frequently produced relief of pain, but they often failed to produce a constant lowering of the free acidity. The acidity was lower in only 11 per cent of the cases after karaya, in 15 per cent after Sippy No. 1 powder, in 23 per cent after amphojel and in 18 per cent after the acid-bismuth mixture. It was higher than the control acidity in 21, 25, 16 and 14 per cent respectively. Sippy No. 1 powder produced complete neutralization for the duration of the test in 10 per cent of the cases and amphojel in 8 per cent. The Sippy powder, moreover, produced marked fluctuations and the greatest rise in the acidity. The fact that relief of pain is frequently obtained without definite or constant neutralization of acidity demonstrates that antacid action is not the sole factor responsible for the relief. Relief can most probably be explained on a lessening of gastric tension. The latter occurs whenever anything is placed in the stomach, probably explaining the beneficial results in the ulcer patients from the use of frequent meals alone. From the results of fractional aspirations in order to prevent the irritating effect of fluctuations in acidity, Sippy powder would have to be given at almost half hour intervals. Patients should do best on that medication which during the fractional test gives either continuously lower acidity or the least fluctuations in acidity in either direction. Ulcer therapy is not based solely on decreasing the gastric acidity.

Studies of Gastric Contents.—Hollander and his colleagues describe a method for the quantitative determination of phenol red concentration in specimens of human stomach contents which contain Liebig's extract, bile, mucin and other protein substances—such as would be obtained in the course of a gastric analysis in which phenol red is used as a dilution indicator. All interfering substances are removed adequately for colorimetry, without appreciable loss of the indicator. The reliability of the method was established on individual determinations of 108 mixed specimens, prepared with various proportions of a test meal containing 40 mg. of phenol red per liter. The standard deviation of this distribution was ± 0.22 mg. per liter. The mean error was $+0.006$ and the mode was -0.016 mg. per liter. Although the range of errors was -0.6 to $+0.9$, only four of the 108 error values were greater than ± 0.4, or 1 per cent of the concentration of phenol red in the test meal.

American Journal of Orthopsychiatry, Menasha, Wis.

10:207-428 (April) 1940. **Partial Index**

What Constitutes Abnormality? I. S. Wile, New York.—p. 216.

Role of Visual Defects in Spelling and Reading Disabilities. G. Spache, New York.—p. 229.

Reading Failure and the Child's Security. Mary I. Preston, San Francisco.—p. 239.

Firesetting in Children. Helen Yarnell, New York.—p. 272.

The Psychology of Children Suffering from Organic Disturbances of Cerebellum. Lauretta Bender, New York.—p. 287.

Maternal Attitudes Found in Twenty-Five Cases of Children with Primary Behavior Disorders. Minna Field, New York.—p. 293.

Constructive Values Associated with Rejection. Mildred Burgum, New York.—p. 312.

Clinical Factor Influencing Variations in Intelligence Quotient. N. C. Kephart and A. A. Strauss, Northville, Mich.—p. 343.

Psychoanalytic Experiences in Public School Practice. H. Zulliger, Bern, Switzerland; translated by Gladys V. Swackhamer, Hartsdale, N. Y.—p. 370.

American Review of Tuberculosis, New York

41:531-674 (May) 1940

*Bronchiectasis: Study of Prognosis Based on Follow-Up of 400 Patients. K. M. A. Perry and D. S. King, Boston.—p. 531.

Beginning of Pulmonary Tuberculosis in Adults. H. Malmros and E. Hedvall, Lund, Sweden.—p. 549.

Primary Tuberculous Infection in Adults. H. Malmros and E. Hedvall, Lund, Sweden.—p. 562.

The Story of Tuberculin. H. S. Willis, Northville, Mich.—p. 573.

Tuberculosis Survey of Sugar Plantation in Hawaii. C. L. Wilbar Jr. and G. E. Wall, Ewa, Hawaii.—p. 582.

BCG Immunization: Comparison of Effects of BCG and of Heat Killed Organisms on Course of Subsequent Infection with Virulent Tubercle Bacilli in Guinea Pig. A. A. Liebow, C. G. Burn and W. B. Soper, New Haven, Conn.—p. 592.

Action of Serum, Cells and Blood on Acid-Fast Bacteria in Vitro: I. Absence of In Vitro Bactericidal Power Against Human Tubercle Bacilli or Timothy Bacilli in Serum-Leukocyte Mixtures or Blood of Normal and Immunized Rabbits. J. H. Hanks and B. Evans, Washington, D. C.—p. 605.

Id.: II. Failure to Demonstrate Bactericidal Power in Various Bloods: Relative Advantages of Solid Medium and of Liquid Blood in Demonstrating Viability of Bacilli in Blood. J. H. Hanks and B. Evans, Washington, D. C.—p. 620.

Id.: III. Evidence of Nutritional Basis of the So-Called Bactericidal Action of Rabbit Serum on Mycobacterium Phlei. J. H. Hanks and B. Evans, Washington, D. C.—p. 637.

*Guinea Pig Inoculation with Gastric Contents of Tuberculous Children. E. Rosencrantz and S. Hurwitz, San Francisco.—p. 645.

Bronchiectasis.—According to Perry and King, a follow-up of 400 cases of bronchiectasis under treatment at the Massachusetts General Hospital from 1926 through 1938 showed that in 49 per cent symptoms developed after acute respiratory infections. In 69 per cent the disease started in the first or second decade of life (42 per cent in the first and 27 per cent in the second). Three hundred and thirty-seven patients were traced; of these eighty-four were dead, 188 reported back to the hospital, sixty-five answered a questionnaire and of the sixty-three untraced patients a search through the death records in the Bureau of Vital Statistics showed that none had died in Massachusetts. There is a strong clinical impression that patients in whom bronchiectasis first develops before the age of 10 do not live beyond the age of 40. Statistical evidence supporting this impression is that only 9.4 per cent of the patients in whom bronchiectasis developed in the first decade lived to or are living at the age of 40 or more. Of the fifty-nine patients who reached the age of 40 or more only 15 per cent had their onset in the first decade. The disease may become saccular or involve portions of the lung parenchyma, but it rarely spreads beyond the lobe or lobes originally involved. The mortality rate over a period of twelve years among the nonsurgically treated patients was 26 per cent; 41 per cent of them died within five years of the onset and 15 per cent lived twenty years or longer after the onset. Death of 78 per cent was a direct result of the disease. The mortality rate in the nonsurgical group among the male patients was 36 per cent as compared to 26 per cent among

the female patients. In the saccular type of bronchiectasis the mortality rate was 37 per cent as opposed to 13 per cent in the cylindric type. The operative mortality in 122 lobectomies performed on 116 patients was 3.3 per cent. The working and living capacity of the traced living patients was excellent in 67 per cent of the surgical group and in 38 per cent of the nonsurgical group. The mortality figures in the surgical and nonsurgical groups are not entirely comparable, but it is still evident that lobectomy is the treatment of choice, especially in unilateral disease. Nonsurgical treatment can be palliative only and preventive treatment is limited to measures directed toward reexpansion of collapsed lobes.

Inoculation of Gastric Contents in Diagnosis of Tuberculosis.—Rosencrantz and Hurwitz used the guinea pig (inoculation of gastric contents) method for the diagnosis of pulmonary tuberculosis among 169 consecutive children with positive tuberculin tests. Seventy-six, or 45 per cent, had tubercle bacilli in the gastric contents. Age was an important factor influencing the results. The results were positive in the nine patients up to 1 year of age. The younger the group, the higher were the percentages for bacilli in the gastric contents; the percentages decreased after the age of 5. This is explained by the fact that the tuberculous process in infants is still active and has not had time to heal and become encapsulated. Therefore children less than 2 years old with a positive tuberculin reaction should be considered as having active tuberculosis until proved otherwise by guinea pig inoculation. The incidence of positive observations in the gastric contents differs in the various clinical types of tuberculosis in children. The gastric contents gave positive reactions in all four cases of acute miliary tuberculosis. Among thirty-eight patients with primary pulmonary infiltration thirty-five, or 92 per cent, had tubercle bacilli. Seven of twelve children who had pleural effusion showed tubercle bacilli on lavage. Only seven of twenty-six children with primary tuberculosis with either the parenchyma or a hilus node calcified exhibited positive gastric lavages. Involvement of the hilus nodes alone was observed in sixty-six patients, and of these sixteen yielded tubercle bacilli. There were six cases of extrapulmonary tuberculosis (meningitis and osseous tuberculosis) and the tubercle bacillus was found in the gastric contents in each case. In all these cases x-ray evidence revealed pulmonary involvement, and the pulmonary tuberculosis was considered primary although the symptoms of the complications predominated. The method is of great importance, for in the absence of physical and x-ray signs it may be the only recognizable evidence of active tuberculosis.

Archives of Pathology, Chicago

29:589-740 (May) 1940

So-Called Mixed Tumors of Mammary Gland of Dog and Man, with Special Reference to General Problem of Cartilage and Bone Formation. A. C. Allen, New York.—p. 589.

*Evaluation of Apparently Increased Incidence of Primary Carcinoma of Lung. T. M. Peery, Washington, D. C.—p. 625.

Experimental Studies in Cardiovascular Pathology: I. Pathologic Changes in Organs of Rats Produced by Chronic Nitrite Poisoning. W. C. Hueper and J. W. Landsberg, New York.—p. 633.

*Incidence of Primary Carcinoma of Lung: Review of Yale Autopsy Protocols, 1917 to 1937. P. D. Rosahn, New Haven, Conn.—p. 649.

Dissecting Aneurysm of Aorta in Experimental Atherosclerosis. T. Leary and S. Weiss, Boston.—p. 665.

Behavior of Tubercle Bacilli Following Their Intravenous Injection into Resistant Animal (Rat). N. C. Oswald, New York.—p. 678.

Primary Carcinoma of Lung.—Peery suggests that statistics on the probable increase of primary carcinoma of the lung are misleading for the following reasons: 1. Prior to 1900 primary carcinoma of the lung was probably diagnosed less frequently than it actually occurred because of the belief that the tumor was exceedingly rare. Most of the tumors of this type were considered metastatic, probably erroneously. 2. Possibly the diagnosis of pulmonary cancer is now made more frequently than is justifiable. Involvement of the bronchial mucosa is not a reliable criterion as metastases to the bronchial mucosa are relatively common. The success of surgical operation and of the application of radium and x-rays in eliminating accessible primary growths, while the secondary tumors remain viable and growing, places an obligation on the clinician and the pathologist to evaluate carefully the changes in every case. 3. The abandonment of the diagnoses "endothelioma of the pleura," "oat cell tumor of the mediastinum" and "tumor of the superior pulmonary sulcus" and the placing of these tumors in the classification of primary carcinoma of the lung, have enlarged the group considerably. These tumors appear to the author to be correctly classified as primary carcinoma of the lung, but the change has swollen the statistics rather than increased the incidence of the disease. Undoubtedly primary carcinoma of the lung is quite common, but apparent increase in its incidence should not be accepted as an actual increase until due allowances are made for the pendulum to come to rest.

Incidence of Primary Carcinoma of Lung.—Rosahn presents new data which show that the increase in the incidence of carcinoma of the lung is not only apparent but real. Among 4,114 persons examined post mortem from Sept. 22, 1917, to Dec. 31, 1937, only 2,968 of whom were more than 20 years of age, 435 carcinomas were found in 425 persons. From 1917 to 1927 there were ten primary pulmonary tumors, or 7.35 per cent of the 136 carcinomas encountered during this period. This compares with thirty-three primary pulmonary cancers seen from 1928 to 1937, or 11.04 per cent of the 299 cancers observed. From 1917 to 1927 carcinoma of the lung was the fifth most frequent tumor. In the following decade it rose to second place. With the exception of prostatic carcinoma, carcinoma of the lung was the only one to increase appreciably during the second of the two ten year periods under consideration. The increasing incidence of primary cancer of the lung is further enhanced by the demonstration that it alone of all tumors had a significant positive raising trend. Analysis of certain factors (improved clinical and pathologic methods of diagnosis, increased attention to this neoplasm, increase in the span of human life and no comparable increase in cutaneous tumors), often cited as evidence that cancer of the lung has shown only a relative increase, has exerted little or no influence on the statistically significant increase in primary carcinoma of the lung found at necropsy in the New Haven Hospital, and it is concluded that the observed increase is real and absolute. Indirect evidence appears to justify the additional conclusion that the real increase in primary carcinoma of the lung observed in this postmortem material is characteristic also of the population at large.

Journal Industrial Hygiene & Toxicology, Baltimore

22:157-198 (May) 1940

Serial Chest Roentgenograms of 3,179 Office Employes, 1926-1938. H. H. Fellows, New York.—p. 157.

Dermatitis from Cashew Nut Shell Oil. J. G. Downing and S. W. Gurney, Boston.—p. 169.

Ventilation of Trichlorethylene Degreaser. W. N. Witheridge and H. T. Walworth, Detroit.—p. 175.

Field Determinations of Carbon Disulfide in Air. F. J. Viles, Boston. —p. 188.

Journal of Lab. and Clinical Medicine, St. Louis

25:669-778 (April) 1940. **Partial Index**

Distribution of Free and Conjugated Sulfanilamide and Sulfapyridine Between Corpuscles and Plasma in Both Human and Rabbit Blood. L. Hansen, Philadelphia.—p. 669.

Note on Level of Glucose and of Nonfermentable Reducing Substances in Therapeutic Insulin Shock. W. H. Forbes and T. Czarski, Baltimore.—p. 679.

Effect of Sulfanilamide on Cross Matching of Blood: Preliminary Report. S. Kreinin, Brooklyn, with technical assistance of Frances A. Hamblen and Lucy Porcelli.—p. 690.

Protection Against Rabies: I. Effect of Frequency of Dosage of Vaccine on Immunity. J. M. Moss, Indianapolis.—p. 702.

Transfusion of Blood from Artificially Immunized Donor in Treatment of Chronic Bacillary Dysentery. R. Turell, New York.—p. 706.

Animal Tissue Reaction to Particulate Copper Stearate. P. T. Knies, Columbus, Ohio.—p. 726.

Distribution of Sulfanilyl-2-Aminopyridine in the Body. H. Chinn and J. Bellows, Chicago.—p. 735.

I. Studies of Liver Function in Health and Disease: Observations on Simple and Accurate Method for Quantitative Determination of Bile Salts in Urine and Bile. L. M. Morrison and W. A. Swalm, Philadelphia.—p. 739.

Tolerance of Diabetic Persons for Dextrose During Various Times of the Day. M. Wishnofsky, A. P. Kane, W. C. Spitz and C. S. Byron, Brooklyn.—p. 754.

Difficulties Encountered in Test for Standardization of Toxin Used Against Scarlet Fever. Betty S. Kolchin, New York.—p. 762.

Journal of Nervous and Mental Disease, New York

91:557-696 (May) 1940

Colloid (Paraphysial) Cyst of Third Ventricle with Rupture Into Caudate Nucleus and Internal Capsule. C. P. Larson, Fort Steilacoom, Wash.—p. 557.
Regression in Catatonia. G. S. Sprague, White Plains, N. Y.—p. 566.
Beriberic Neuromyeloses. A. Austregesilo, Rio de Janeiro, Brazil.—p. 579.
A Genetic Approach to the Problem of Stammering. A. B. Berman and G. J. Train, Brooklyn.—p. 590.
Progressive Facial Hemiatrophy: Report of Case with Attacks of Syncope and Gynandromorphism. M. O. Wolfe and M. L. Weber, Dearborn, Mich.—p. 595.
Heredopathic Combination of Congenital Deformity of Nose and of Myoclonic Torsion Dystonia. L. Benedek and E. Rakonitz, Budapest, Hungary.—p. 608.
Studies in Delayed Awakening in Insulin Shock Therapy (Sakel): II. Blood Pressure Observations and Their Possible Interpretation. G. W. Robinson and G. W. Robinson Jr., Kansas City, Mo.—p. 625.

Journal of Neurophysiology, Springfield, Ill.

3:191-282 (May) 1940

Electric Responses Derived from Superior Cervical Ganglion with Micro-Electrodes. P. O. Therman, A. Forbes and R. Galambos, Boston.—p. 191.
Effect of Cortical Lesions on Affective Pupillary Reactions. B. Ury and E. Oldberg, Chicago.—p. 201.
Postural Reflexes and Grasp Phenomena in Infants. B. L. Pacella, Brooklyn, and S. E. Barrera, New York.—p. 213.
Action of Ether and Nembutal on Nervous System. P. Heinbecker and S. H. Bartley, St. Louis.—p. 219.
Degeneration and Regeneration of Sympathetic Synapses. W. C. Gibson, Oxford, England.—p. 237.
Studies of Motor Performance After Parietal Ablations in Monkeys. Margaret A. Kennard and M. M. Kessler, New Haven, Conn.—p. 248.
Somatic and Autonomic Reflexes in Spinal Monkeys. A. L. Sahs and J. F. Fulton, New Haven, Conn.—p. 258.
Nerve Activity Accompanying Fasciculation Produced by Prostigmine. R. L. Masland and R. S. Wigton, Philadelphia.—p. 269.
Effects on Respiration, Blood Pressure and Gastric Motility of Stimulation of Orbital Surface of Frontal Lobe. P. Bailey and W. H. Sweet, Chicago.—p. 276.

Maine Medical Association Journal, Portland

31:115-150 (May) 1940

Medicine Today. L. P. Gerrish, Lisbon Falls.—p. 115.
Nature of Neuroses. M. Marquardt, Augusta.—p. 118.
Cardiac Emergencies and Their Treatment. G. R. Brow, Montreal.—p. 122.
One Thousand Tuberculin Tests with Purified Protein Derivative. E. A. Greco and Mary G. Gordon, Portland.—p. 128.

Missouri State Medical Assn. Journal, St. Louis

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Cancer of Uterus: Early Diagnosis and Treatment. G. D. Royston, St. Louis.—p. 189.
Underwater Therapy in Chronic Arthritis. V. E. Frazier, Kansas City.—p. 192.
Fractures of Vertebrae During Metrazol Therapy. L. L. Tureen and J. A. Key, St. Louis.—p. 194.
Value of Electrocardiogram in Diagnosis. G. Asher, Kansas City.—p. 197.
Syphilitic Cardiovascular Disease. C. C. Dennie, Kansas City.—p. 198.
Pericarditis. R. E. Myers, Joplin.—p. 200.
Coronary Artery Disease. H. M. Parker, Kansas City.—p. 202.
*Beverage Alcohol and Heart Disease. F. C. Helwig, Kansas City.—p. 204.
Functional Heart Disease. W. M. Kinney, Joplin.—p. 206.

Beverage Alcohol and Heart Disease.—Helwig believes that alcohol by itself is of no significance in the etiology of angina pectoris, essential hypertension, arteriolonephrosclerosis and coronary sclerosis. There is considerable evidence to show that it may have a definite retarding effect on the development of arteriosclerosis and atherosclerosis. It has been stated that alcohol may be of extreme benefit in coronary disease. According to Paul White 1 or 2 ounces (30 or 60 cc.) of whisky, brandy or rum may give relief from angina pectoris within a few minutes. There is no clinical or pharmacologic evidence that would suggest that alcohol alone ever produces heart disease. The symptoms may be produced by a deficient diet in the absence of alcohol, and often they may take place long after the ingestion of alcohol has ceased. The mere fact that symptoms such as polyneuritis, pellagroid lesions and cardiovascular dysfunction disappear on continuous alcoholic intake with simultaneous administration of vitamin B should make it obvious that alcohol can be only a factor. Pellagra and various types of cardiac disease are known to be associated with specific avitaminosis without alcoholism and will clear up in addicts with proper vitamin therapy in the face of continued alcoholism. Patients with acute and chronic alcoholism and heart disease should be subjected to an extremely critical and searching analysis of their previous dietary habits before a conclusion regarding the etiologic background of the cardiac condition is reached. "Beer drinker's heart" is an obsolete term and should be abandoned.

Northwest Medicine, Seattle

39:157-198 (May) 1940

Lipiodol versus Air as Aid in Diagnosis of Protrusion of Intervertebral Disk. S. N. Berens, Seattle.—p. 160.
Vitallium in Internal Fixation in Bone Surgery. J. I. Tuell, Seattle.—p. 163.
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Exclusion Operation for Carcinoma of Colon. W. C. Speidel, Seattle.—p. 179.
Ovarian Cysts Complicating Pregnancy. C. M. Helwig, Seattle.—p. 180.
Female Pseudohermaphroditism. P. R. Rollins, Seattle.—p. 181.
Convulsions Associated with Nitrous Oxide-Ether Anesthesia. W. B. Cook, Seattle.—p. 182

Texas State Journal of Medicine, Fort Worth

36:1-70 (May) 1940

Bone Disease in Children: Radiologic Features. J. B. Johnson and H. M. Anspach, Galveston.—p. 5.
Id.: Orthopedic Features. G. W. N. Eggers, Galveston.—p. 7.
Surgical Treatment of Uterovaginal Prolapse. L. W. Pollok, Temple.—p. 15.
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Observations on Etiology of Polycythemia Vera. W. B. Adamson and J. E. Storey, Abilene.—p. 26.
Cutaneous Precancerosis. L. E. Edens, Austin.—p. 29.
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Expanding Field of Public Health Activities. J. N. Baker, Montgomery, Ala.—p. 43.
New Developments in Crippled Children's Work. J. J. Brown, Austin.—p. 47.

Virginia Medical Monthly, Richmond

67:261-326 (May) 1940

Largest Collection of Medical Literature Ever Assembled: Story of the Army Medical Library, with Notes of Virginians Who Have Directed It. E. E. Hume, Carlisle, Pa.—p. 261.
Remarks on Diagnosis and Treatment of Angina Pectoris. E. G. Scott, Lynchburg.—p. 273.
Esophageal Diverticulum. R. L. Payne and R. D. Jones Jr., Norfolk.—p. 278.
Treatment of Sciatica. D. M. Faulkner, Richmond.—p. 287.
Experience with Thyroid Disease in Western Virginia. R. P. Bell, Staunton.—p. 293.
Endocrinology Briefs: Ovaries. J. P. Lynch, Richmond.—p. 296.
Use of Unna's Paste in Treatment of Varicose Ulcer. W. B. Marbury and R. L. Jackson, Washington, D. C.—p. 298.
Analysis of Cesarean Section at University of Virginia Hospital. J. M. Nokes, University.—p. 300.
Lithopedion with Calcified Placenta: Case Report. P. W. Oden and H. C. Lee, Richmond.—p. 304.
Sulfanilamide in Burns. B. C. Grigsby, Bonny Blue.—p. 306.

West Virginia Medical Journal, Charleston

36:193-240 (May) 1940

Function of Joints in Relation to Fracture Treatment. R. H. Kennedy, New York.—p. 193.
Role of Psychiatry in Pediatrics. J. Basman, Charleston.—p. 199.
What May Be Seen in the Eyes. R. A. Tomassene, Wheeling.—p. 202.
Progress in Orthopedic Surgery, with Discussion of Some of the Newer Principles of Treatment. A. R. Lutz, Parkersburg.—p. 205.
Probable Effects of Testosterone on Prostatic Hypertrophy. C. J. Reynolds, Bluefield.—p. 211.
Some Diseases of the Mouth. C. W. Stuart, Chicago.—p. 215.
Surgical Problem of Gallbladder Disease. L. Gage, Princeton.—p. 220.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

1:719-756 (May 4) 1940

Insulin Deficiency and Insulin Inefficiency. H. P. Himsworth.—p. 719.
Strain Variations in Resistance of Streptococcus Viridans to Sulfonamide Compounds. R. H. A. Swain.—p. 722.
Splinting Fractures of Humerus. K. O. Parsons and A. T. Hart.—p. 726.
Diphtheria Prophylaxis: Optimal Dosage and Technic in Use of Alum Precipitated Toxoid. J. T. Lewis.—p. 728.
Benzedrine Sulfate: Its Use to Interrupt Avertin Anesthesia. J. Boyd.—p. 729.

Journal of Physiology, Cambridge

98:1-140 (March) 1940. **Partial Index**

Glycogen and Calcification. G. E. Glock.—p. 1.
Effect of Temperature on Mechanical Response and Viscosity and Oxygen Consumption of Unstriated Muscle. M. Sadashiva Rao and I. Singh.—p. 12.
Composition of Alveolar Air. I. F. S. Mackay.—p. 73.
Effect of Gravity on Blood Pressure of Cat. O. G. Edholm.—p. 79.
Renal Excretion of Inulin and Creatinine by Anesthetized Dog and Pump-Lung-Kidney Preparation. J. A. Shannon and F. R. Winton.—p. 97.
Inactivation of Adrenalin by Phenolases. H. Blaschko and H. Schlossmann.—p. 130.

Lancet, London

1:819-864 (May 4) 1940

Death in the First Month and the First Year. C. McNeil.—p. 819.
Treatment of Certain Types of External Hernias. C. P. G. Wakeley.—p. 822.
Lumbar Curve in Women: Changes Produced by Displacement of Center of Gravity. L. K. Klinderová.—p. 827.
*Insulin Suppositories. B. Brahn.—p. 829.
*Subendocardial Hemorrhages in Shock. H. L. Sheehan.—p. 831.
*Wounds of Chest Treated by Artificial Pneumothorax. C. H. Kretzschmar.—p. 832.

Insulin Suppositories.—Brahn points out that insulin introduced into the rectum is destroyed by the tryptic digestive ferments. His object was to protect the insulin against these ferments, which can act in an alkaline medium only, by adding acids to it and to accelerate its absorption by adding substances which increase the surface tension. Suppositories of theobroma oil were used as the vehicle for these substances. The tests were carried out on rabbits and on healthy human beings. The blood sugar estimations were made by the Hagedorn-Jensen method at intervals of from fifteen to thirty minutes, beginning from thirty to forty minutes after the introduction of the suppository. About 150 tests on rabbits and as many on human beings were carried out. Suppositories consisting of theobroma oil and insulin had no effect on rabbits or on man. The addition of acid preserved the efficacy of the insulin in suppositories of theobroma oil. A combination of lactic and palmitic acid proved most effective. However, since palmitic acid melts only at 60 C., it was necessary to melt it first with theobroma oil in the proportion of 15 to 85; this yielded a mixture with a melting point of 33 C. The addition of saponin increased the intensity and duration of the action of an acid-containing insulin suppository in rabbits and man. The action of insulin introduced into suppositories sets in soon and attains its maximum after thirty to forty minutes, at the end of which time the action again subsides rapidly. Larger doses of insulin increase not only the intensity but also the duration of the action. The effect of insulin suppositories may be varied by increasing the insulin content in an otherwise unchanged combination, by modifying the quantity of acid and saponin without changing the amount of insulin or by varying the quantity of each substance. Wuhrmann tested insulin suppositories clinically and found them to be of value (*Schweiz. med. Wchnschr.* **69**:787 [Sept. 2] 1939; abstr. THE JOURNAL, Nov. 11, 1939, p. 1844).

Subendocardial Hemorrhages in Shock.—Sheehan asserts that subendocardial hemorrhages are among the most regular pathologic aspects of shock due to obstetric causes. The material reviewed is from the routine obstetric necropsies performed in the Glasgow Royal Maternity and Women's Hospital during the last two and a quarter years in which a systematic search for the hemorrhages was made in every case. Shock resulted from the usual obstetric causes: dystocia in sixteen cases, retained placenta in twelve, uteroplacental apoplexy in nine, rupture or inversion of the uterus in five, and other conditions, including those in which hemorrhage played some part, in ten. Subendocardial hemorrhages, localized to the left side of the interventricular septum and less often also to the musculi papillares and trabeculae of the left ventricle, are almost invariably present in obstetric deaths from shock, except when the patient dies rapidly, that is within an hour. The author thinks that subendocardial hemorrhages cannot be considered as merely one aspect of generalized damage to the capillaries. They are not to be confused with the widespread hemorrhages in mucosae and serosae, which some authors record in animal experiments but which have not been found in these cases of shock in human beings. They cannot be dismissed as "agonal lesions" which may occur in any kind of death; on the contrary, they are restricted to certain special types of death. The close relationship between their incidence in cases of shock and the duration from the onset of shock to the time of death suggests that they usually take some time to develop. In postmortem examination on patients who die some days after recovery from shock there are usually no remaining lesions, or, if present, they are quite small. It appears, therefore, that the hemorrhages take place not in the lesser degrees of shock but only in severe or fatal cases. The fact that they are also found in deaths from various kinds of cerebral lesions suggests a possible nervous mechanism for their production in shock. They are presumably a postmortem indication that a vascular disturbance in this region has been present for some time before death, but the relationship of this vascular disturbance to the syndrome of shock is not yet elucidated.

Wounds of Chest Treated by Artificial Pneumothorax.—According to Kretzschmar, the treatment of chest wounds by artificial pneumothorax was introduced into the Italian army in 1916 by Morelli. During the Spanish war the author saw death from intrathoracic hemorrhage after a comparatively small chest wound. Hemorrhage is intensified or prolonged by the negative pressure in the pleural cavity. The hemothorax does not check the hemorrhage, for if the wound is in the upper part of the lung the hemothorax does not reach the level of the wound. Spontaneous cessation of pulmonary hemorrhage is more probably due to the pneumothorax which usually accompanies penetrating wounds of the chest. A traumatic pneumothorax is not an indication for operation unless it is valvular or complicated by an infected effusion or by progressive hemorrhage from the lung. When there is progressive pulmonary hemorrhage, and when there are foreign bodies in the lung, a complete artificial pneumothorax should be induced to cause collapse of the lung. The hemothorax, if large, should be cleared out by thoracocentesis as completely as possible, because its absorption takes a long time, causes thickening of the diaphragm and pleural adhesions, and impedes the cardiac action and the expansion of the sound lung, and there is a risk of pyopneumohemothorax with a doubtful prognosis. The artificial pneumothorax has its therapeutic effect on the wound of the lung, stops or reduces the hemorrhage from the lung, prevents the obliteration of the sinuses and the formation of adhesions between the visceral and parietal pleura, protects the lung from further damage due to movement of foreign bodies and prevents inflammation of the lung caused by these foreign bodies. Artificial pneumothorax therefore should have a permanent place in thoracic surgery, especially in war time.

Practitioner, London

144:453-548 (May) 1940

Pleurisy and Allied Disorders. W. H. Wynn.—p. 453.
Treatment of Asthma. J. N. Cruickshank.—p. 465.
Problems of Pulmonary Tuberculosis in the Adolescent. W. E. Lloyd.—p. 478.
Industrial Lung Disease: Diagnosis and Treatment. H. H. Moll.—p. 487.
Diagnosis and Treatment of Enlarged Mediastinal Glands in Children. P. Williams.—p. 499.
Prescribing in Wartime. H. N. Linstead.—p. 506.
Modern Therapeutics: XI. Diuretics and Urinary Antiseptics. E. B. Mayrs and T. H. Crozier.—p. 516.

Presse Médicale, Paris

48:361-384 (April 10-13) 1940

Effect of Chronic Intoxication with Chlorine Impregnated Atmosphere on Experimentally Induced Tuberculosis of Guinea Pig. F. Arloing, E. Berthet and J. Viallier.—p. 361.
Collective Oxygen Inhalators Fed by Liquid Oxygen. Cot and Genaud.—p. 361.
Angina Pectoris Due to Thyroid Dysfunction. J.-C. Mussio-Fournier and J.-T. Fischer.—p. 363.
*Late Relapses in Unilateral Tuberculous Cavities Apparently Healed by Thoracoplasty. A. Bernou, H. Fruchaud and M. Gautier.—p. 366.

Late Relapses After Thoracoplasty.—Bernou and his associates report twenty instances (8.26 per cent) of late recurrence after 242 thoracoplasties performed for unilateral pulmonary cavities. In three of the twenty cases the contralateral lung showed involvement, in seven surgical intervention was not extensive enough and in the other ten pulmonary collapse had been unsatisfactory. Seven of the patients made a good recovery after subsequent management with rest and rib resection on a larger scale. Only four of the ten patients were regarded by the authors as offering a doubtful prognosis because of weak walls after extraperiosteal resection. Observation time extended from fifteen months to eight years for the group of cases of severe late reactivation and from seven to sixteen months for the group in which thoracoplasties were performed with extraperiosteal resection with deficient wall collapse. Relapses were noted in 3.7 per cent of the cases presenting subperiosteal resection in which the field of operation had been unduly narrowed. A 30.8 per cent reactivation of infection was noted in thoracoplasty with extraperiosteal resection showing too rapid a recovery. In apparently healed pulmonary lesions subsequent trauma caused to the sensitive lung by effort or cough may reactivate former lesions. No relapse occurred in any of 242 cases at the site of the primary lesion or directly under it when surgical intervention was carried out effectively with proper parietal collapse.

Revue Belge des Sciences Médicales, Louvain

12:1-32 (Jan.) 1940

Circulatory Inversion in Kidney. E. Lauwers.—p. 1.
*Adeno-Acanthoma of Cervix Followed Two Years Later by Papilliferous Adeno-Epithelioma of Uterus: Case. P. Desaive.—p. 12.
Acromegaloidism in Puberty: Case. M. Schachter.—p. 24.

Adeno-Acanthoma of Cervix and Adeno-Epithelioma of Uterus.—Desaive discusses a case in which an adenoacanthoma of the cervix was followed two years later by an adenocarcinoma of the uterus, the two neoplasms disclosing differentiated microscopic pictures. The patient, 44 years old, with a normal history, presented a cervical tumor which was successively treated with radium (vagina, intra uterum) and roentgen rays. She remained in excellent health until, a few years later, a true papilliferous adeno-epithelioma of the uterus was diagnosed. Hysterectomy was performed, which left her apparently in perfect health. The author believes that the two tumors belong to the category of multiple growths and arose independently of each other. The effect of the roentgen rays in canceration of tissue is not excluded. Diagnosis and biopsy should not confine themselves to the cervix, even if this alone is affected, but include more extensive examinations of the uterine area. Hysterectomy is the method of choice. If irradiation is employed, it should induce a complete and permanent atrophy of the mucosa of the uterus.

Chirurg, Berlin

12:145-176 (March 15) 1940. **Partial Index**

Care in Base Hospital for Persons Injured by Bombs: Experiences in China. C. Reimers.—p. 145.
Treatment of Injuries of Male Urethra. F. Voelcker.—p. 152.
Preparatory and After-Treatment of Patients Operated on for Rectal Cancer. H. H. Westermann.—p. 156.
*Digitalis in Treatment of Wounds. H. Baron.—p. 160.

Digitalis in Treatment of Wounds.—Baron studied the effect of digitalis on wounds, particularly on those failing to respond to the customary treatments. Digitan was applied either in a 10 per cent solution or as a 10 or 20 per cent ointment. A compress saturated with the solution is placed on the wound and a layer of cotton saturated with the solution placed over it. This dressing is changed after twenty-four hours. Zinc paste is applied to the surrounding healthy tissue to prevent maceration. Digitan ointment is used first in the stronger and later in the weaker concentration. Ointment bandages, changed daily, were employed in the treatment of new, extensive burns. The ointment is especially advantageous in facial burns because it is odorless. Ointment bandages, remaining in place for about a week, were applied to wounds that had improved under digitan compresses. Digitan ointment bandages in combination with plaster of paris casts were left in place for several weeks. This therapy has been employed in forty-eight cases, including postoperative and post-traumatic suppurating wounds, burns, carbuncles, crural, decubital and x-ray ulcers, necrosis caused by contrast medium and osteomyelitis. The advantages of digitalis treatment of wounds are: 1. It improves blood perfusion and purification of wounds. 2. It inhibits inflammation and stimulates granulation. 3. It stimulates epithelization. The author suggests that these effects are the result of improved blood flow in the capillaries of the wound brought about by the action of digitalis on the cells of the capillary wall. A bactericidal effect is probable but has not been definitely proved.

Deutsche medizinische Wochenschrift, Leipzig

66:281-308 (March 15) 1940. **Partial Index**

*Treatment of Acute Lobar Pneumonia with Sulfapyridine: Report of 303 Cases. C. Hegler.—p. 281.
Comparative Investigations on Action of Various Diseptals (Sulfanilamides) in Treatment of Gonorrhea. H. Löhe and R. Wawersig.—p. 283.
Chemotherapy in Gynecology. W. Stoeckel.—p. 286.
Treatment of Rheumatism with Radium Irradiations. Stoia and Heda Stoia.—p. 291.

Sulfapyridine in Acute Lobar Pneumonia.—Hegler reports 303 cases of acute lobar pneumonia treated with sulfapyridine. The initial dose was 2 Gm. Nausea and vomiting frequently followed and the drug was then administered rectally. On the second, third and subsequent days, adults were given daily from 3 to 4 Gm. in fractionated doses. The total dose, administered in the course of from five to seven days, varied between 15 and 25 Gm. Better results were obtained with these large doses than with the more prolonged administration of smaller doses. Children tolerate sulfapyridine well and can be given from one half to one tablet of 0.5 Gm. of the drug from two to four times daily. In addition to the sulfapyridine the patients were given cardiac and circulatory stimulants. The drug proved successful for patients of all ages and against the different types of pneumococci. Especially noteworthy is the favorable action on type III (mucosus), which does not respond to serotherapy. Even cases in which there was involvement of several lobes, with bacteremia, responded well. The treatment was the more effective the earlier the medicament was administered. Fifteen patients died, but five of these were already moribund when hospitalized and the treatment of six more was begun too late to be effective. Thus it may be said that only four of 293 patients died in spite of treatment with sulfapyridine. The author concludes that sulfapyridine is the method of choice in the treatment of acute lobar pneumonia.

Vestnik Khirurgii, Leningrad

58:479-622 (Dec.) 1939. **Partial Index**

Tetanus Prophylaxis. A. M. Zabludovskiy.—p. 485.
Complications of Serum Prophylaxis of Tetanus. E. V. Usoltseva.—p. 494.
*Procaine Hydrochloride Block in Acute Ileus. G. M. Novikov.—p. 506.
Procaine Hydrochloride Block Treatment of Carbuncles and Furuncles of Upper Lip and Corner of Mouth. S. A. Beylin.—p. 513.
Experimental Chronic Cystic Mastitis and Bleeding Breast. Ya. E. Sorin.—p. 517.
Significance of Mucous Plug in Injuries of Stomach and Bowel. S. S. Sharimenyan.—p. 528.
*Undescended Testes: Operative Indications. A. Ya. Dukhanov.—p. 558.

Procaine Hydrochloride Block in Acute Ileus.—Between 1936 and 1938, 139 patients with acute intestinal obstruction were admitted to the surgical clinic of Novikov (Leningrad). Sixty-three of these were operated on, while seventy-six (55 per cent) got well on a conservative regimen whose main feature was the lumbar procaine hydrochloride block as practiced by Vishnevskiy. The patient is brought direct from the admitting room into the operating room. From 50 to 100 cc. of 0.25 per cent

procaine hydrochloride is injected into the right or the left renal fossa. In forty-six of the seventy-five cases the procaine hydrochloride block alone resulted in from thirty to sixty minutes in a diminution of pain, passage of flatus and a copious bowel movement. In twenty-nine the block relieved the pain and caused some passage of flatus but no stool. Siphoning enemas brought about passage of feces. Five patients were treated with enemas alone without result. Induction of the procaine hydrochloride block caused flatus and stool in from twenty to sixty minutes. Of twenty-two patients with obstruction due to postoperative adhesions, seventeen were relieved by the procaine hydrochloride block and three by the block supplemented by enemas. The modus operandi of the lumbar procaine hydrochloride block is probably to be seen in the removal of the irritating factor, result of anesthesia of a wide network of the vegetative nervous system. The method offers the possibility of preoperative recognition and of effective treatment of functional ileus. The method may likewise prevent the transition of a functional ileus into a mechanical one.

Undescended Testes.—Dukhanov reports on forty-four patients with undescended testes, thirty-three of whom were operated on and eleven of whom were treated conservatively. Follow-up was possible in twenty cases. Increase in the size of testes which were brought down was noted in only four cases. In twelve the testes were atrophied, in five of these almost completely. Orchidopexy per se apparently did not exert a stimulating influence on growth of the testis. The occurrence of complications of a retained testis is too rare to constitute an indication for operative intervention. Complaints of pain of continuous or spasmodic character on the part of the patient constitute, in the author's opinion, an absolute indication for intervention because it suggests a tendency on the part of the retained testis to strangulation or to torsion of the spermatic cord. Sixteen of twenty patients had complete relief from pain. The author's impression, based on his observations and review of the literature, is that the great majority of the ectopic testes descend spontaneously about the time of sexual maturity and considerably later. Such testes not infrequently develop and reach normal size. The favorable effect of treatment with gonadotropic substance on the descent and growth of the testes suggests that the pathogenesis of cryptorchidism is dysfunction of the endocrine apparatus.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

84:1285-1384 (April 6) 1940. **Partial Index**

Thrombosis of Coronary Artery. L. P. Daniels.—p. 1286.
*Changes at Mouth of Esophagus in Plummer-Vinson Syndrome (Dysphagia with Anemia). P. G. Gerlings.—p. 1289.
Evacuation and Measles. H. I. de Ruiter.—p. 1297.
Special Form of Leukemia. J. J. de Jong.—p. 1301.

Esophageal Changes in Dysphagia with Anemia.—According to Gerlings, the concurrence of hypochromic anemia with dysphagia, the so-called Plummer-Vinson syndrome, is often seen first by laryngologists, because dysphagia is generally the chief complaint. The majority of patients are middle-aged women who give a history of several years of dysphagia, the difficulty in swallowing being localized at the level of the larynx. They may have been taking only fluid and strained foods, because solid foods "get stuck in the throat." Examination often discloses a small mouth with rhagades at the corners and a pale oral mucous membrane. The lingual mucosa may be smooth as the result of atrophy of the papillae and, like the buccal mucosa, it may have patches of leukoplakia. There is dryness and perhaps atrophy of the pharyngeal mucosa. The anemia is of the hypochromic type. Koilonychia (spoon nails) is a frequent symptom. Achlorhydria is likewise frequent and in some cases the spleen can be felt. Internal therapy in the form of iron and hydrochloric acid improves not only the anemia but also the dysphagia. The author stresses the value of the x-ray examination and of esophagoscopy in patients with the Plummer-Vinson syndrome. They are essential in ascertaining the nature of the lesions at the mouth of the esophagus, such as stagnation of secretion in the pyriform sinus and just above the mouth of the esophagus, superficial ulceration and stenosis by scarring (in bands or in circular form). The possibility of carcinoma must always be kept in mind.

Acta Medica Scandinavica, Stockholm

104:1-233 (April 23) 1940. **Partial Index**

*Further Observations on Zoster and Spinal Diseases. M. Kobro.—p. 1.
Contribution to Question of Nervous and Muscular Substratum of Muscle Tone. Gösta Häggqvist.—p. 8.
Microdetermination of Ester Sulfate in Blood and Pus. B. Norberg.—p. 21.
Pernicious Anemia and Exophthalmic Goiter. T. Stenstam.—p. 29.
Clinical Observations on Course and Prognosis of Lymphogranulomatosis Benigna (Schaumann), Particularly in Regard to Pulmonary Lesions. T. Bruce and E. Wassén.—p. 63.
Osteopoikilosis with Dermatofibrosis Lenticularis Disseminata. M. Sjöholm.—p. 108.
Cerebral Manifestations of Lymphogranulomatosis Benigna (Schaumann) and Uveoparotid Fever (Heerfordt). B. Roos.—p. 123.
Schaumann's Disease (Benign Lymphogranulomatosis) with Erythrodermic Patches and Iridocyclitis as Dominant Clinical Symptoms. G. Nordin.—p. 131.
*Effect of Prolactin on Secretion of Milk in Women in Puerperium and for First Few Months After Parturition as Well as in Newborn Babies. K. G. Kaijser.—p. 158.
Hippuric Acid Test as Means for Determining Hepatic Function. A. J. Quick.—p. 216.

Zoster and Spinal Diseases.—Kobro observed six patients with vertebral lesions in whom zoster developed in segmental relation to these defects. One patient presented zoster scars in the third and fourth cervical segment, and x-ray examination disclosed ankylosis of the second and third cervical vertebrae. Another patient had destruction of the fifth thoracic vertebra due to myelomatosis, and zoster developed in the fifth thoracic segment. A third patient had Hodgkin's disease with involvement of the sixth thoracic vertebra, and zoster appeared in the sixth thoracic segment. Another patient had spondylolisthesis between the fourth and the fifth lumbar vertebra and zoster developed in the fourth lumbar segment. The objection may be made that the concurrence of zoster with vertebral lesions is a coincidence. However, each added case makes it seem more probable that a causal relation exists. The six cases of regional zoster with vertebral diseases have been found among a limited number. A methodical search was made for patients with vertebral lesions and zoster that was not in segmental relationship but none were found. Zoster in patients with vertebral lesions was always in segmental relation to the vertebral defects. It thus appears that a vertebral lesion may give rise to a regional zoster and, since vertebral lesions may exist for a time without symptoms, the appearance of zoster should direct attention to the possibility of a vertebral lesion. The fact that zoster is not a common but only an exceptional complication of vertebral lesions indicates that a ganglionic lesion alone cannot provoke zoster but that there must be another factor, and it is believed that this is the specific virus of zoster. The nonspecific lesion seems only to prepare the milieu for the specific virus of zoster.

Prolactin and Secretion of Milk.—Kaijser experimented with prolactin, the lactation-promoting hormone of the anterior lobe of the hypophysis. Prolactin is a hypothetical hormone which is not prepared in a chemically pure form but is obtained in an extract from the pituitary. The preparation used was an extract of sheep pituitary, free from demonstrable thyrotropic, adrenotropic and gonadotropic factors. It was administered intramuscularly in quantities measured in daily pigeon doses. The author studied the amount of milk produced by 249 healthy women who did not receive prolactin. Studies on the effect of prolactin given during the first month after parturition revealed that no real increase in the supply of milk could be demonstrated except in cases in which prolactin was administered within a week of parturition. Prolactin was given also to women in whom hypogalactia appeared during a later stage of lactation. The results do not provide definite proof that prolactin has any real effect on the milk supply during the later stages of lactation. The author studied the effect of prolactin on the production of witch's milk in infants during the first few months of life. These babies have been under the same hormone influences as their mothers, and their mammary tissue may be imagined to have undergone similar preparation. Thus, if prolactin is of real value to lactation in the mother, its administration to babies during the first few months of life should provide some evidence as to its properties. In a number of cases the author succeeded in demonstrating a slight increase in the glandular tissue and in a few cases the appearance of milky fluid in small quantities on mild pressure on the breasts.